Azzazi

Anesthesia, Intensive Care
& Pain Therapy

SPOTLIGHTS ON ANESTHESIA, INTENSIVE CARE & PAIN THERAPY



SECOND EDITION
Vol .2

HESHAM EL AZZAZI

SPOTLIGHTS ON ANESTHESIA, INTENSIVE CARE & PAIN THERAPY

Second Edition

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Volume 2

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PREFACE

Response to the first edition of this book has been extremely good. In the years since it was written, positive feedback has come from residents, practitioners, colleagues and others in the medical field.

However, advances and changes in the availability of equipment and drugs, together with changes in clinical practice, made a new edition necessary.

Anesthesiologists are increasingly responsible for the development and care of patients preoperatively and postoperatively and in the recognition and management of those who are critically ill, as well as the continuing essential role that many anesthesiologists play in treating and helping patients live with chronic pain problems. So, as with the first edition, the overall aim of this book is to present anesthesia and its related skills in terms that will help practitioners worldwide to deal effectively and safely with the needs of surgical, severely ill and critically ill patients .

The second edition of spotlights on anesthesia is presented in a completely colored format, organized into three volumes. Most of the chapters in this edition have been completely rewritten (including **1306 new illustrations and images and 500 new tables**), and there are new chapters on physics, anesthetic machines and equipment, pharmacology and pain management. The references have been extensively updated, with emphasis on recent reviews and clinical practice guidelines.

Although this edition has been completely revised, it is still based on the same principles of simplicity and practicability, using many color illustrations and photographs.

The format is designed to provide easy access to information presented in a concise manner. I have tried to eliminate as much as possible superfluous material. The style of the chapters varies. This is deliberate; some relate more to basic principles, physiology, pharmacology, etc. Others are more practical in nature, discussing the principles of anesthetic techniques for certain high-risk situations.

To reduce the variability that is the bane of multi-author texts, I am the sole author and I have personally edited every chapter in this book, to ensure consistency of style. Consequently, this book is a reflection of the workload involved that has taken me four years to complete.

I would really appreciate your feedback on my book. I am sure that even after careful review and editing, it won't be free of errors or perfectly clear to everyone who reads it. If you see ways that I can correct or improve the book, please let me know by e-mail at: **hesham@azzazianesthesia.com**. If you like certain aspects of the book, I would appreciate hearing about that, too.

Finally, I would like to say that trained people are the most valuable resource in medicine, and what you practice is what you read and learn.
So, if this book helps in any way, in improving the level of training, knowledge and practicing of anesthesia among anesthesiologists, then it will have fully achieved its goal.

Hesham El-Azzazi

DEDICATION

To all my family, to my wife and lovely children,
Ahmed and Hana and to the souls of my beloved ones

ACKNOWLEDGMENT

I would never have been able to complete this book without the friendship, support and knowledge of all my professors and colleagues. Every day, I feel how lucky I am to have been able to work with them.

Thanks to my residents and students, who drive me to improve with every minute, and my sincere appreciation to all my patients as well.

I am specially grateful to *Dr. Ahmed El Hanafi*, for his meticulous work with the illustrations, to *Dr. Sahar Talat* for her linguistic efforts, and *Dr. Lobna Habib* for reviewing all radiological material enclosed in this book.

I would also like to thank the readers of the first edition of this textbook who offered me excellent feedback that helped me add several new features to this edition.

Finally, thank you to my family, my wife and children. Thank you for reminding me daily how beautiful the world is, – even after a disenchanting day at work.

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RESPIRATORY DISEASES

12

- Physiological considerations
- Effect of anesthesia on respiration
- Preoperative patient evaluation
- Preoperative investigations
- Preoperative patient preparation

Postoperative respiratory complications and failure

- Obstructive pulmonary diseases
- Restrictive pulmonary diseases
- Disorders of the pleura and mediastinum
- Pulmonary embolism
- Acute respiratory failure
- Prone position and prone ventilation of the lungs
- Unilateral decreased breath sounds during general anesthesia
- Pulmonary atelectasis and collapse
- Drowning and near-drowning

Physiological Considerations

Cellular Respiration

1- Aerobic Metabolism: (Aerobic i.e., use O_2)

Carbohydrates, fats, and proteins are utilized by cells for production of adenosine triphosphate (ATP) (figure 12-1). **One glucose** molecule gives **38 molecules of ATP aerobically.**

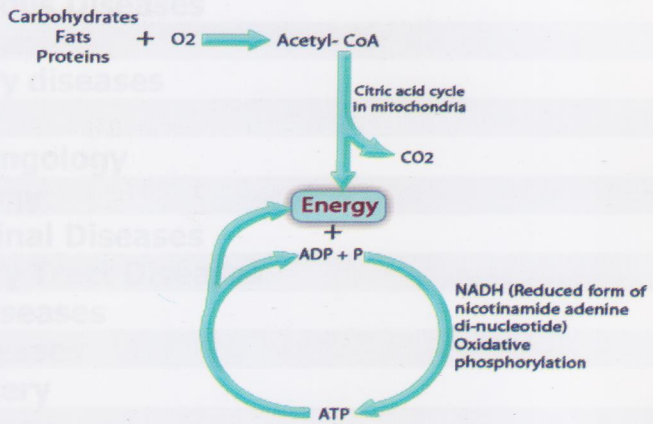


Figure 12-1: Aerobic metabolism

Respiratory Quotient (RQ)

It is the ratio of total CO_2 production ($\dot{V}CO_2$) to O_2 consumption ($\dot{V}O_2$). It is generally indicative of the primary type of fuel being utilized.

RQ for - carbohydrates is 1.0 where there is more CO_2 production.
- lipids is 0.7
and - proteins is 0.8

Normal $\dot{V}CO_2$ is 200 mL/min while normal $\dot{V}O_2$ is 250 mL/min.

2- Anaerobic Metabolism: (An-aerobic i.e., not use O_2)

In case of unavailability of oxygen (hypoxia), carbohydrates are utilized producing lactic acidosis and ATP anaerobically. **One glucose** molecule gives **2 molecules of ATP anaerobically** (figure 12-2).

Carbohydrates → Pyruvate → Lactic acid (causing lactic acidosis) + ATP

Figure 12-2: Anaerobic metabolism

The point at which tissues change from aerobic to anaerobic metabolism due to unavailability of oxygen, e.g., during respiratory failure or shock, is defined as the **anaerobic threshold**.

Functional Respiratory Anatomy

1- Muscles of Respiration:

a- During Normal Inspiration:

• The **diaphragm** is responsible for **60-75%** of the change in chest volume, while **external intercostal muscles** are responsible for **25-40%** of the change in chest volume. Since vital capacity (4-6 L in an adult) far exceeds the normal tidal volume (500 mL), it is apparent that **individuals can survive indefinitely if they lack either one of these muscular systems provided the other is intact** e.g., in cesarean section with T_2 level of spinal anesthesia, there is block of the intercostals, but the diaphragm is intact; therefore, the patient can breathe adequately. Also, cervical epidural anesthesia produces bilateral phrenic nerve block which blocks the diaphragm, but the intercostals are intact; therefore, the patient can breathe adequately.

During an Increased Inspiratory Effort: e.g., during exercise, both muscular systems are needed as above in addition to • **Sternocleidomastoid** which assists in rib elevation.

• **Scalene** which prevents inward displacement of upper ribs.

• **Pectoralis** which assists chest expansion when arms are placed on a fixed support.

b- During Normal Expiration in Supine Position:

Expiration is **passive** (with some abdominal muscle contraction).

During an Increased Expiratory Effort or in Erect Position: e.g., during airway obstruction as in chronic obstructive pulmonary diseases (COPD) or asthma, expiration is **active** with the action of the following muscles: • **Abdominal muscles** (rectus abdominis, external and internal oblique and transversus).

• **Internal intercostal muscles** which aid downward movement of ribs.

N.B.: Some **pharyngeal muscles maintain patency of the airway** (they are not usually considered respiratory muscles) such as:

• **Genioglossus** which keeps the tongue away from the posterior pharyngeal wall.

• **Levator palati, tensor palati, palato-pharyngeus, and palato-glossus** which keep the soft palate away from the posterior pharyngeal wall.

2- Tracheo-Bronchial Tree:

• The function of the tracheo-bronchial tree is to conduct gas to the alveoli. Each branch divides into two smaller branches. There are **23 divisions.** This arrangement is called **dichotomous division**. It is arranged as follows, from the larger to the smaller, "Trachea, bronchi, bronchioles, terminal bronchioles, respiratory bronchioles, alveolar duct, alveolar sac". Each alveolar sac contains an average of 17 alveoli. The mucosal epithelium makes a gradual transition from ciliated columnar to cuboidal and finally to flat alveolar epithelium.

• **Gas exchange** can occur only across the flat epithelium which begins to appear on **respiratory bronchioles (generations 17-19).**

3- Alveoli:

The Alveolar Wall is formed of two walls:

• **Thick side (support wall)** for structural support of the alveoli. It is formed of:

- Alveolar epithelial cells and their basement membrane (figure 12-3).
- A pulmonary interstitial space which contains (elastin, collagen, and nerve fibers).
- A basement membrane.
- Capillary endothelial cells.

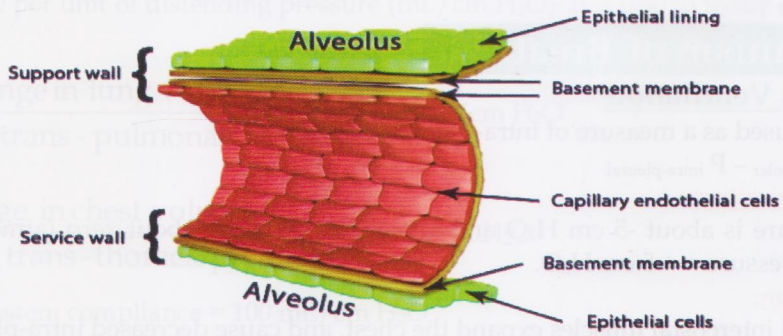


Figure 12-3: The alveolar wall

• **Thin side (service wall)** for gas exchange. Its thickness is 0.4 µm. It is formed of:
- Alveolar epithelial cells.
- One basement membrane.
- Capillary endothelial cells.

Respiratory Epithelium: is of two types:

Type I Pneumocytes	Type II Pneumocytes
• Many • Flat cells • Can not divide • Can not resist O_2 toxicity • Form tight junctions (1 mm) which prevent passage of large oncotically active molecules as albumin into the alveoli	• Few • Rounded • Can divide and provide type I cells if the latter are destroyed. • Can resist O_2 toxicity • Contain prominent cytoplasmic inclusions (lamellar bodies) which constitute the surfactant.

Other Cells: are present such as:
• Pulmonary alveolar macrophages.
• Mast cells.
• Lymphocytes.
• APUD cells.
• Neutrophils (in smokers).

4- Pulmonary Circulation:

There are two circulations:
• The bronchial circulation: It arises from the left side of the heart and supplies the tracheo-bronchial tree down to the respiratory bronchioles.
• The pulmonary circulation: It arises from the right side of the heart and supplies lung tissues below respiratory bronchioles (in combination with the alveolar gas).

5- Innervations:

a- Motor: - The diaphragm is supplied by the phrenic nerve "C_{3-5} nerve roots".
- Intercostal muscles are supplied by respective thoracic nerve roots.

N.B.: Cervical cord injuries above C_5 are incompatible with spontaneous ventilation as both the phrenic nerve and intercostal nerves are affected.

b- Sensory: The vagus nerve to the tracheo-bronchial tree.

c- Autonomic:
- **Parasympathetic system:** passes through the vagus via **muscarinic** receptors. It causes bronchospasm, increased bronchial secretions, vasodilation of the pulmonary vessels (mediated by nitric oxide).
- **Sympathetic system:** passes through T_1-T_2 via:
• **α_1 receptors:** They cause bronchospasm, decreased secretions, and vasoconstriction of pulmonary vessels.
• β_2 receptors: They cause bronchodilatation, increased secretions, and vasodilation of pulmonary vessels.
- **Non-adrenergic, non-cholinergic bronchodilator system**: Its neuro-transmitter is vasoactive intestinal peptide.

Basic Mechanism of Breathing

A) Spontaneous Ventilation:

Pleural pressure is used as a measure of intra-thoracic pressure.

$P_{trans\text{-}pulmonary} = P_{alveolar} - P_{intra\text{-}pleural}$

• **At the End of Expiration:**

Intra-pleural pressure is about -5 cm H_2O and alveolar pressure is about zero (atmospheric); therefore, trans-pulmonary pressure = + 5 cm H_2O.

• **During Inspiration:**

The diaphragm and intercostal muscles expand the chest, and cause decreased intra-pleural pressure to -7.5 cm H_2O; therefore, alveolar pressure decreases to – 1 cm H_2O. This creates an alveolar - upper airway gradient which makes gas flow from the upper airway into the alveoli (+ 6.5).

- **At the End of Inspiration:**

Alveolar pressure returns to zero (gas inflow has ceased), but intra-pleural pressure remains decreased. So, trans-pulmonary pressure becomes + 7.5 cm H_2O which sustains lung expansion.

- **During Expiration:**

Diaphragm relaxation occurs; therefore, intra-pleural pressure becomes – 5 cm H_2O. Elastic recoil of the lung occurs; therefore, alveolar pressure becomes + 1 cm H_2O. So, reversal of alveolar-upper airway gradient occurs (+ 6) which makes gas flow out of the alveoli (figure 12-4).

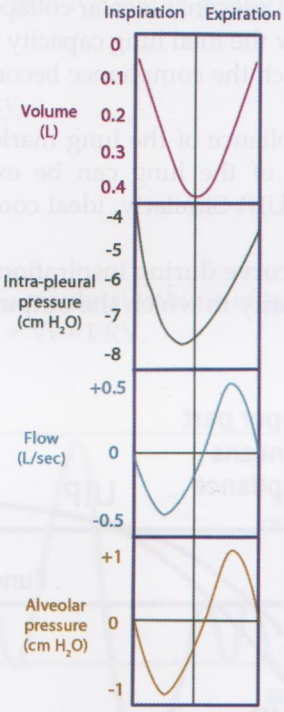


Figure 12-4: Alveolar and intrapleural pressures

B) Mechanical Ventilation:

Most forms of mechanical ventilation produce intermittent positive airway pressure at the upper airway.

- **During Inspiration:**

Gas flows into the alveoli until alveolar pressure reaches that in the upper airway.

- **During Expiration:**

The positive airway pressure is removed or decreased; therefore, the gradient reverses and pressures gas to flow out of alveoli.

Mechanics of Ventilation

Compliance (C):

It is sometimes called distendability or stretchability.

It is volume change per unit of distending pressure (mL/cm H_2O). It is due to tissue elasticity and surface tension.

$$C_{lung} = \frac{\text{Change in lung volume}}{\text{Change in trans-pulmonary pressure}} = 200 \text{ mL/cm } H_2O$$

$$C_{chest} = \frac{\text{Change in chest volume}}{\text{Change in trans-thoracic pressure}} = 200 \text{ mL/cm } H_2O$$

Total respiratory system compliance = 100 mL/cm H_2O

$$\frac{1}{C_{total}} = \frac{1}{C_{chest}} + \frac{1}{C_{lung}}$$

Static Pressure-Volume Curve (Compliance Curve)

There are 2 critical regions in which pulmonary compliance is very poor:

- The first region is slightly above the residual volume and denotes a **critical opening volume** whereby recruitable alveoli have the propensity to collapse during tidal breathing. **Cyclic opening and closing** of these alveolar units has been implicated as a cause of **ventilator-induced lung injury**. The determination of the **lower inflection point (LIP)** (sometimes called Pflex) on the static pressure-volume curve allows the clinician to set the positive end expiratory pressure (PEEP) to 2 cm H_2O above this critical opening volume to prevent alveolar collapse and promote recruitment.
- The second region is slightly below the total lung capacity where the compliance of the lung is again becomes poor. The point above which the compliance becomes poor is called **upper inflection point (UIP).**

Between the LIP and UIP, the compliance of the lung markedly improves where the curve becomes steep, therefore; the ideal volume of the lung can be extracted from this curve as the volume contained between the LIP and the UIP. Similarly, ideal compliance can be derived from the slope of this curve (figure 12-5).

The curve shows **hysteresis** where the curve during inspiration is not the same curve during expiration. Hysteresis is a special form of non-linearity in which the output differs depending on whether the input signal is increasing or decreasing.

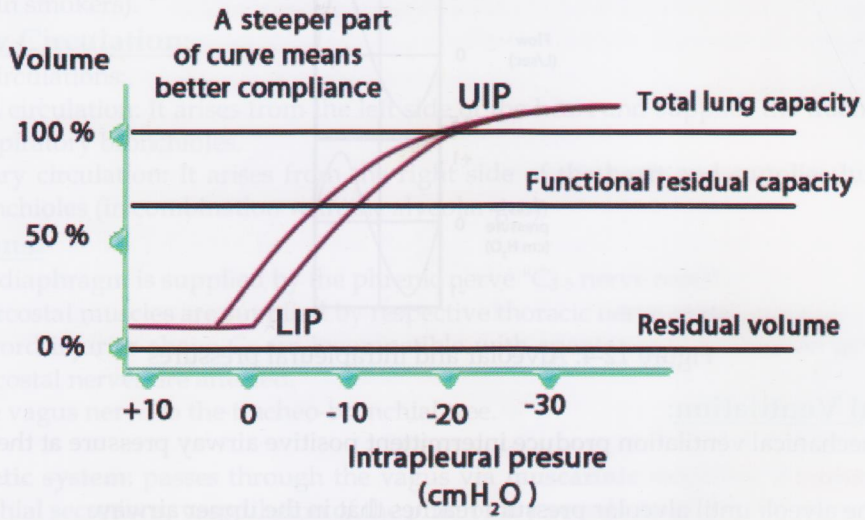


Figure 12-5: Static pressure volume curve

Static Lung Volumes

Definitions:

The normal values of all volumes differ according to the patient's sex, age, height (they are more related to the height than the weight of the patient).

They include:

Tidal Volume (V_t): It is each normal quite breathing = 7 – 10 mL/kg.

Inspiratory Reserve Volume (IRV): It is the maximal additional volume that can be inspired above V_t.

Inspiratory capacity: It equals IRV + Vt.

Expiratory Reserve Volume (ERV): It is the maximal additional volume that can be expired below V_t.

Residual Volume (RV): It is the volume remaining in the lung after maximal expiration.

Functional Residual Capacity (FRC):

•It is the volume remaining after normal expiration i.e., at the resting expiratory position (resting lung volume). It equals RV + ERV.

Factors Decreasing FRC:

1. Prone position.
2. Supine, head down position.
3. Anesthesia intraoperatively.
4. Abdominal and thoracic surgery postoperatively.

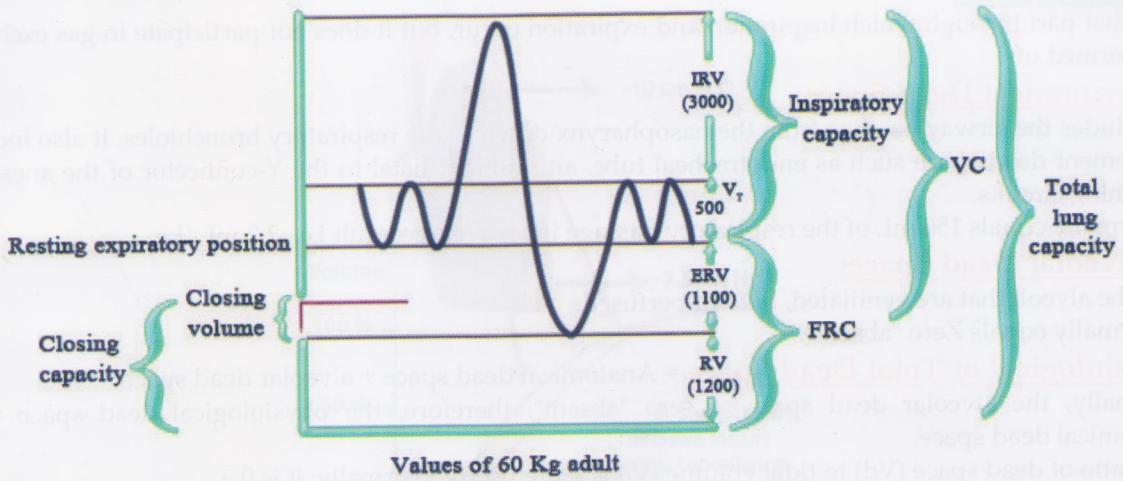
5. Pulmonary fibrosis: It decreases lung compliance.
6. Pulmonary edema: It decreases lung compliance.
7. Obesity.
8. Abdominal swelling e.g., pregnancy, tumor, and ascites; they decrease chest compliance.
9. Thoracic cage distortion: It decreases chest compliance.
10. Reduced muscle tone.

Factors Increasing FRC:

1. Increased intra-thoracic pressure e.g., positive end expiratory pressure (PEEP) or continuous positive airway pressure (CPAP).
2. Upright posture.
3. Emphysema: It decreases lung elasticity.
4. Asthma.
5. Young age.
6. Male gender.
7. Increased height.
8. Decreased weight.

Vital Capacity (VC) (figure 12-6)**:** It is the maximal volume of gas that can be exhaled following maximal inspiration = 50-55 mL/kg. It equals IRV + Vt + ERV.

Total Lung Capacity: It equals VC + RV.



N.B.: Capacity i.e. 2 or more volumes

Figure 12-6: Static lung volumes and capacities

Closing Volume (CV):

It is the volume of the lung at which small airways "respiratory or terminal bronchioles" (without cartilages) **in the dependent parts of the lung** begin to collapse during expiration.

Normally, it is less than the FRC, but greater than the RV. In normal young people, it is about 10% of the vital capacity. Normally, the FRC acts as a buffer between the lung's volume and the closing volume i.e., FRC prevents the lung from falling into the closing volume range. After exhalation of normal tidal volumes, there is plenty of air remaining in the lung, preventing it from shrinking to the closing volume.

It can be demonstrated by expiration to the RV, which is inevitably followed by a sigh to re-expand the collapsed lung.

Closing Capacity (CC):

It is the closing volume + residual volume.

CC is measured by trace gas (xenon^{133}) which is inhaled near residual volume and then exhaled from total lung capacity or by single breath nitrogen test.

Factors Affecting CC:

1- Age and position: **CC increases by age** as at 44 years CC equals FRC in supine position, at 66 years CC is ≥ FRC in upright position.

Actually, CC is not affected by posture but the above changes are due to decreased FRC and not due to increased CC.

If CC is > FRC, the alveoli are perfused, but not ventilated (i.e., intrapulmonary shunt) causing hypoxemia. Therefore, normally there is a decrease in PaO_2 with age.

2- Pathology: CC is increased with chronic smoking, obesity, chronic bronchitis, left ventricular failure and pulmonary edema.

Thoracic Gas Volume:

It is the total volume of gas present in the thorax whether in free communication with the airway or not.

It increases in: • Obstructive airway diseases and emphysema.
• Lung tumor and cysts.

In both, the air is stopped distal to the occluded airway.

Dynamic Lung Volumes

- **Forced Vital Capacity (FVC):** It measures vital capacity as expiration is as hard and as rapid as possible.
- **Forced expiratory volume in the 1st second (FEV_1):** It is the volume that is expired in one second during FVC.
- **FEV_1/FVC ratio:** It is proportional to the degree of airway obstruction. It is normally = 80%.

More details about pulmonary functions test measurements are discussed in the chapter of "Monitoring during Anesthesia & Intensive Care".

Dead Space

It is that part through which inspiration and expiration occur, but it does not participate in gas exchange. It is formed of:

1. Anatomical Dead Space:

It includes the airway passage from the nasopharynx down to the respiratory bronchioles. It also includes equipment dead space such as endotracheal tube, and tubing distal to the Y-connector of the anesthesia breathing circuits.

It normally equals 150 mL of the respiratory passage in an average adult i.e., 2.2 mL/kg.

2. Alveolar Dead Space:

It is the alveoli that are ventilated, but not perfused.

It normally equals Zero "absent".

Physiological or Total Dead Space = Anatomical dead space + alveolar dead space

Normally, the alveolar dead space = Zero "absent"; therefore, the physiological dead space = the anatomical dead space.

The ratio of dead space (Vd) to tidal volume (V_t) is more useful. Normally, it is 0.3.

Factors affecting the dead space:

a- Factors Increasing the Dead Space:

1- Upright posture.
2- Neck extension.
3- Advanced age.
4- Positive pressure ventilation, PEEP, and increased airway pressure.
5- Anticholinergics which cause bronchodilatation.
6- Decreased pulmonary perfusion e.g., pulmonary emboli or hypotension.
7- Lung diseases such as emphysema or cystic fibrosis.

b- Factors Decreasing the Dead Space:

1- Supine posture.
2- Neck flexion.
3- Intubation.

Anatomical dead space can be measured by single-breath nitrogen test, while physiological dead space is measured by modified Bohr's equation

$$Vd/Vt \text{ ratio} = \frac{PaCO_2 - P\acute{E}CO_2}{PaCO_2}$$

Where: $PaCO_2$ = CO_2 tension in the arterial blood. It is obtained by an arterial sample.
$P\acute{E}CO_2$ = CO_2 tension in the expired air. It is obtained by collecting mixed expired gas in a Douglas bag and subjecting this to analysis or by using capnography.
Vt = the tidal volume.

Surface Tension

It tends to collapse the alveoli

Laplace's law states that pressure (within an alveolus) $= \frac{2 \times \text{Surfacetension}}{\text{Radius}}$

The pressure is high in small bubbles, so if in continuity with a larger bubble, the smaller bubbles will empty completely.

Surfactant (dipalmitoyl lecithin) secreted from type II pneumocytes decreases surface tension. As when the alveolus decreases in size, the concentration of surfactant is increased in the surface layer of fluid which in turn effectively decreases surface tension and decreases the tendency of the alveolus to collapse. The reverse occurs when the alveolus increases in size; therefore, there will be a relatively constant pressure within the alveolus.

Ventilation/Perfusion Matching

Distribution of Ventilation:

Inspired gas is directed towards **the dependant parts of lungs** due to the differences in the compliance of different parts of lung. These differences in compliance are because the weight of the lung produces less negative intra-pleural pressure at the base compared with the apex. Therefore, the lung at the base is less expanded with smaller resting volume. It expands better on inspiration and has better compliance and better ventilation (figure 12-7).

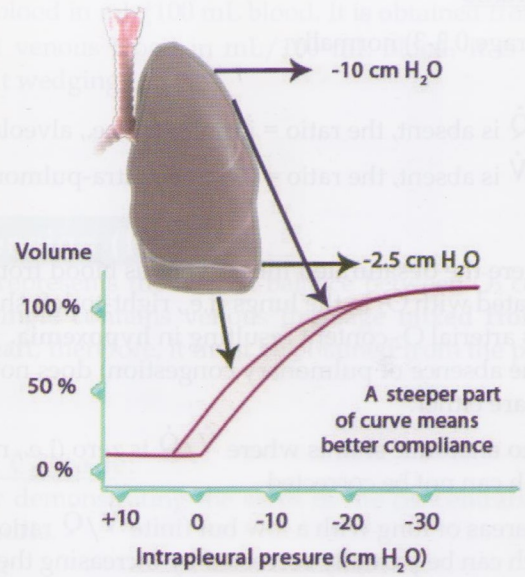


Figure 12-7: Distribution of ventilation

Distribution of Pulmonary Perfusion:

The lower (dependent) portions of the lung receive greater blood flow than the upper (nondependent) areas. This is due to the effect of **gravity**.

Each lung can be divided into **3 classic West's zones.**

- **Zone I (upper zone):** (**PA** > Pa > Pv)

It represents the alveolar dead space i.e., there is ventilation without blood flow. It does not occur normally, but occurs in states with low pulmonary artery pressure such as hypovolemia, blood loss, and under anesthesia and with increased alveolar pressure as in positive pressure ventilation.

- **Zone II (middle zone):** (Pa > **PA** > Pv)

Pulmonary capillary flow is intermittent and varies during respiration. The flow is proportional to difference between pulmonary artery pressure and airway pressure.

- **Zone III (lower zone):** (Pa> Pv > **PA**)

Pulmonary capillary flow is continuous and proportional to the arterial-venous pressure gradient (figure 12-8).

Recently, zone IV has been added which accounts for increased interstitial pressure in the dependent zones causing decreased perfusion.

Where PA = alveolar or airway pressure
Pa = pulmonary artery pressure
Pv = pulmonary vein pressure

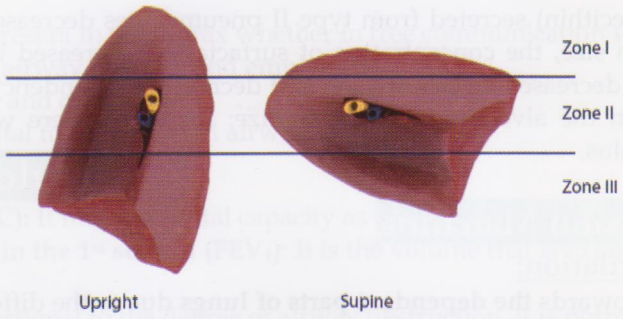


Figure 12-8: Distribution of pulmonary perfusion

Ventilation ($\dot{V}$)/Perfusion ($\dot{Q}$) Ratio

$$\frac{\text{Ventilation}}{\text{Perfusion}} = \frac{5\ \text{L/min}}{5\ \text{L/mi}} = 1 \text{ (average 0.3-3) normally.}$$

If $\dot{V} > \dot{Q}$, the ratio is > 1 and if $\dot{Q}$ is absent, the ratio = infinity (∞) i.e., alveolar dead space.

If $\dot{Q} > \dot{V}$, the ratio is < 1 and if $\dot{V}$ is absent, the ratio = Zero i.e., intra-pulmonary shunt.

Shunt

Definition: It is the process where the desaturated mixed venous blood from the right heart **returns** to the left heart without being resaturated with O_2 in the lungs (i.e., right-to-left shunt).

Effects: It dilutes and decreases arterial O_2 content resulting in **hypoxemia.**

N.B.: A left-to-right shunt (in the absence of pulmonary congestion) does not produce hypoxemia.

Types: Intrapulmonary shunts are either:

1- An absolute shunt: It refers to anatomic shunts where $\dot{V}/\dot{Q}$ is zero (i.e., no ventilation).
This produces hypoxemia which can not be corrected.

2- A relative shunt: It refers to areas of lung with a low but finite $\dot{V}/\dot{Q}$ ratio.
This produces hypoxemia which can be partially corrected by increasing the inspired O_2 concentration.

Venous Admixture

Definition: It is the amount of mixed venous blood that has to be mixed with pulmonary end-capillary blood to account for the difference in O_2 tension between arterial and pulmonary end-capillary blood (figure 12-9).

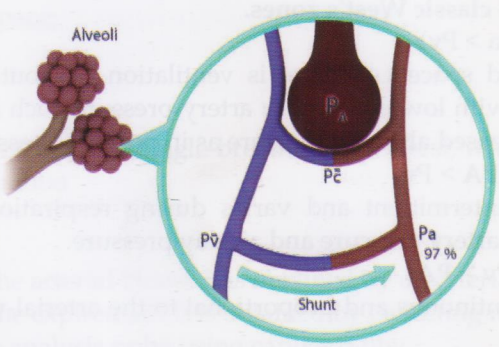


Figure 12-9: Venous admixture

If there is no shunt (i.e., no venous admixture), the O_2 tension in pulmonary end-capillary blood will be equal to that in arterial blood.
Pulmonary end-capillary blood is considered to have the same concentration as alveolar gas (P_AO_2).
Actually, there is a difference between PAO_2 and PaO_2 which is due to:
1- **Venous admixture:** Dilution of pulmonary end-capillary blood by blood which has bypassed the lung as the bronchial circulation, the thebesian veins (which drain directly into the heart) and cardiac anomalies.
2- The diffusion gradient across the alveolar capillary membrane.
3- **Intra-pulmonary shunt:** Blood which has come from areas of the lung with low ventilation e.g., atelectasis, pneumonia, or pulmonary edema i.e., $\dot{V}/\dot{Q}$ ratio < 1. It is the mixed venous blood which is not exposed to alveolar gas and does not mix with oxygenated blood.
The venous admixture in normal individuals (physiological shunt) is typically less than 5%. The PA-a gradient is 5-10 mm Hg.

$$\text{Virtual shunt fraction } \frac{\dot{Q}s}{\dot{Q}t} = \frac{Cc'_{=2} - CaO_2}{Cc'O_2 - C\bar{v}O_2}$$

Where:
$C\acute{c}O_2$ = O_2 content of end pulmonary capillary blood in mL/100 mL blood. It is obtained through a pulmonary artery catheter during wedging.
CaO_2 = O_2 content of arterial blood in mL/100 mL blood. It is obtained from an arterial catheter.
$C\bar{v}O_2$ = O_2 content of mixed venous blood in mL/100 mL blood. It is obtained through a pulmonary artery catheter slowly without wedging.
$\dot{Q}s$ = Venous admixture.
$\dot{Q}t$ = Total cardiac output.

Mixed Venous O_2 Tension ($P\bar{v}O_2$)

It is normally 40 mm Hg. It represents the overall balance between O_2 consumption and O_2 delivery. A true mixed venous blood sample contains venous drainage **mixed from the superior vena cava, the inferior vena cava and the heart**; therefore, it must be obtained from the pulmonary artery catheter.

Gas Exchange

A) Oxygen: The Oxygen Cascade:

It is a convenient method for demonstrating the steps of the concentration gradient for O_2 between the atmosphere and the mitochondria.
N.B.: 1 KPa = 1% = 7.6 mm Hg

1- Dry Atmospheric Air:

Air contains 21% O_2 concentration.
Partial pressure of inspired O_2 (PiO_2) = Barometric pressure (P_B) x FiO_2
= 760 mm Hg x 0.21 = **159.6 mm Hg**

2- Humidified Air at 37 °C:

Humidification occurs by upper airway causing addition of water vapor which in turn decreases PiO_2 i.e., the inspired gas is diluted by the presence of water vapor.
Therefore, $PiO_2 = (P_B - P_{H2O}) \times FiO_2$
$= (760 - 47) \times 0.21 =$ **149.73 mm Hg**
Where; P_{H2O} is the saturated vapor pressure of water at body temperature (37°C). Normally, it is 47 mm Hg (figure 12-10).

3- Ideal Alveolar Gas (A):

In alveoli, the inspired gases are mixed with residual alveolar gas from previous breaths, O_2 is taken up and CO_2 is added. With a normal diet, respiratory quotient (RQ) is less than 1 because CO_2 production is slightly less than O_2 consumption.

$$RQ = \frac{CO_2 \text{ production}}{O_2 \text{ consumption}} = \frac{200 \text{ mL/min}}{250 \text{ mL/mi}} = 0.8$$

The final alveolar O_2 tension (PAO_2) can be estimated from the **ideal alveolar gas equation**

$$PAO_2 = PiO_2 - \frac{PACO_2}{RQ} = \textbf{100- 110 mm Hg}$$

As the difference between $PACO_2$ and $PaCO_2$ is very small, the equation can be written as follows:

$$PAO_2 = PiO_2 - \frac{PaCO_2}{RQ}$$

$PAO_2 = 149.73 - 40/0.8 = 149.73 - 50 = 99.73$ mm Hg

Respiratory quotient (RQ) is usually not measured. It is assumed to be 0.8 at room air with normal diet and 1 at O_2-enriched mixture.

If $PaCO_2$ increases to > 75 mm Hg, hypoxia occurs (i.e., PAO_2 is < 60 mm Hg) at room air; therefore, high inspired O_2 concentration is required to prevent development of hypoxia in presence of hypercapnia.

A simple method of approximating PAO_2 to mm Hg is to multiply % of inspired O_2 concentration by 6, thus at 40%, PAO_2 is 6 x 40 = 240 mm Hg.

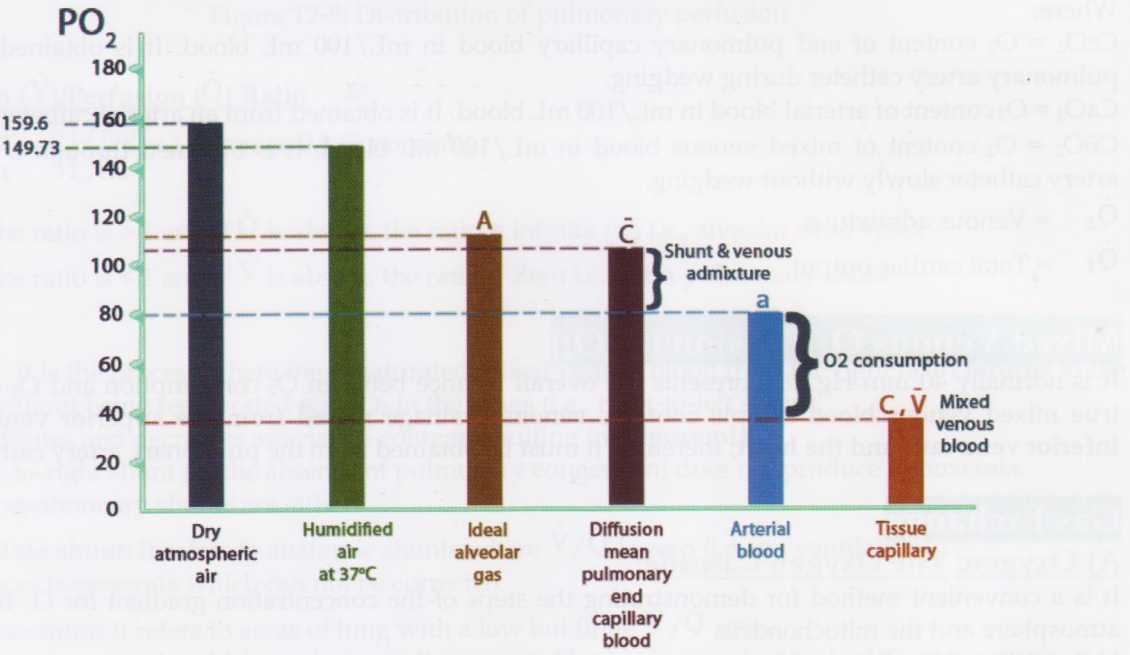


Figure 12-10: The O_2 cascade

4- Mean Pulmonary End-Capillary Blood (c̄):

Pulmonary end-capillary O_2 tension ($Pc̄O_2$) may be considered identical to PAO_2 as PAO_2 - $Pc̄O_2$ gradient is very small or minute.

$Pc̄O_2$ is nearly 100 mm Hg.

$Pc̄O_2$ is dependent on:

1- The rate of O_2 diffusion across the alveolar-capillary membrane. It is facilitated by:

- The large capillary surface area in the alveoli.
- The small thickness of the alveolar-capillary membrane which is 0.4-0.5 μm.

2- Enhanced O_2 binding to hemoglobin (Hb) at saturation above 80%.

3- Transit time via capillaries:

$$= \frac{\text{Pulmonary capillary blood volume}}{\text{Pulmonary blood flow}} = \frac{70 \text{ mL}}{5000 \text{ mL/mi}} = 0.8 \text{ second}$$

Maximum $Pc̄O_2$ is usually attained after only 0.3 second providing a large safety margin.

O_2 uptake from alveolar gas to blood is normally limited and affected by pulmonary blood flow (and O_2 binding to Hb), and not by O_2 diffusion across the alveolar-capillary membrane (O_2 diffusing capacity) because the latter has a large safety margin.

$$O_2 \text{ diffusing capacity } (D_LO_2) = \frac{O_2 \text{ uptake}}{PAO_2 - P'cO_2}$$

N.B.: Because $PćO_2$ cannot be measured accurately, measurement of carbon monoxide diffusion capacity instead is used to assess gas transfer across the alveolar-capillary membrane.

Because carbon monoxide has a very high affinity for Hb, carbon monoxide tension in the pulmonary end capillary blood (PćCO) can be considered zero.

$$\text{Therefore, Carbon monoxide diffusing capacity } (D_LCO) = \frac{\text{Carbon monoxide uptake}}{\text{Alveolar carbon monoxide tension}}$$

Decreased D_LCO represents a decrease in gas transfer across the alveolar-capillary membrane. This may occur in: • abnormal $\dot{V}/\dot{Q}$ ratios.

- Extensive destruction of alveolar-capillary membrane.
- Very short capillary transit times.

5- Arterial O_2 Tension (PaO_2):

Due to presence of shunt and venous admixture, PaO_2 is less than $PćO_2$. PaO_2 decreases with age. $PaO_2 = 102 - \frac{Age}{3}$ **= 60-100 mm Hg**

6- Tissue (Interstitial) PO_2:

Due to O_2 consumption, Tissue or interstitial PO_2 is decreased to **15-40 mm Hg** in normal conditions, where the mixed venous blood oxygen tension ($PῡO_2$) becomes also 40 mm Hg.

7- Intracellular (Mitochondrial) PO_2:

The intracellular (mitochondrial) PO_2 is about **15 mm Hg at the arterial side and 1.5 mm Hg at the venous end of capillaries with average 5 mm Hg**. This corresponds to an O_2 concentration of 0.15 mL/L inside cells. This demonstrates that tissues of the human body normally operate in an oxygen deficient environment (figure 12-11).

This means that cells can tolerate severe degrees of hypoxemia without evidence of inadequate tissue oxygenation i.e., without anaerobic metabolism.

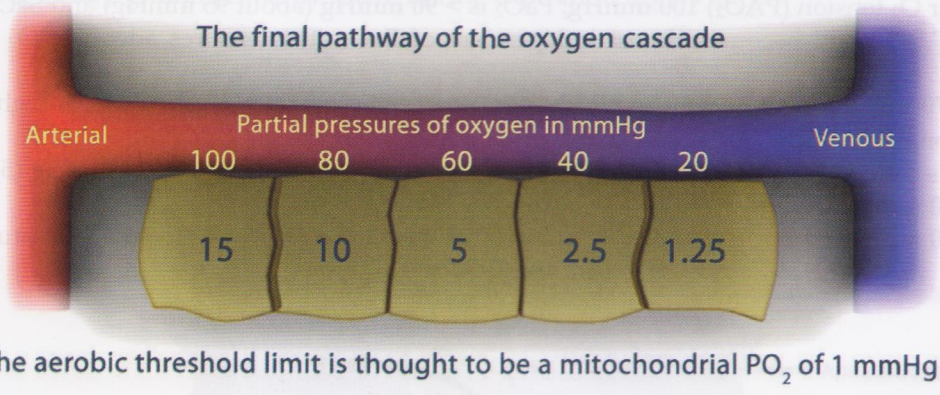


Figure 12-11: The final pathway of O_2 cascade

B) CO_2:

It passes in reverse direction from the mitochondria to the cell cytoplasm, extracellular fluid, venous blood and finally to the alveoli. CO_2 is carried in the blood as dissolved gas, as bicarbonate, and as a small amount bound to Hb as carbamino-hemoglobin. Unlike the oxy-Hb dissociation curve, the **dissociation curve for CO_2 is essentially linear**.

1- Mixed Venous CO_2 Tension ($PῡCO_2$):

It is normally about 46 mm Hg.

2- Alveolar CO_2 Tension ($PACO_2$):

It represents the balance between total CO_2 production ($\dot{V}CO_2$) and alveolar ventilation ($\dot{V}_A$) or elimination. $PACO_2$ is determined by **the alveolar carbon dioxide equation**

$PACO_2$ or $PaCO_2 = \dot{V}CO_2/\dot{V}_A \times k$ Where; k is a constant (0.863) that corrects units.

Clinically, $PACO_2$ is more dependent on alveolar ventilation than $\dot{V}CO_2$ because CO_2 output does not vary appreciably under most circumstances.

3- Pulmonary End-Capillary CO_2 Tension ($PćCO_2$):

It is virtually identical to $PACO_2$ (as with O_2). The diffusion rate for CO_2 across the alveolar capillary membrane is 20 times that of O_2.

4- Arterial CO_2 Tension ($PaCO_2$):

It is identical to $PćCO_2$ and $PACO_2$. It is normally 40 mm Hg.

Low $\dot{V}/\dot{Q}$ ratio increases $PaCO_2$ (i.e., hypercapnia)

and high $\dot{V}/\dot{Q}$ ratio decreases $PaCO_2$ (in contrast to O_2).

5- End-Tidal CO_2 Tension ($P_{ET}CO_2$):

Because end-tidal CO_2 is primarily alveolar, $PACO_2$ is identical to $PaCO_2$; therefore, $P_{ET}CO_2$ is used clinically to estimate $PaCO_2$.

$PaCO_2$ - $P_{ET}CO_2$ gradient is normally < 6 mm Hg due to dilution of alveolar gas with CO_2-free gas from non-perfused alveoli (alveolar dead space).

Transport of O_2 in Blood

Oxygen is carried in the blood in two forms; O_2 **chemically combined with hemoglobin (Hb)** and that **physically dissolved in plasma**. Both represent the oxygen content.

O_2 delivery, O_2 uptake, O_2 extraction ratio, and mixed venous O_2 saturation are discussed before in cardiovascular monitoring in the chapter of "Monitoring during Anesthesia & Intensive Care".

Oxy-Hb Dissociation Curve

It shows the relationship between the oxygen tension and the hemoglobin saturation. It is **sigmoid (elongated S)** in shape due to successive oxygenation of the 4 heme groups of the Hb molecule in steps, where there is an increased affinity to O_2 after the 1st heme group is oxygenated (figure 12-12).

Hb saturation: is the amount of O_2 bound, as a percentage of its total O_2-binding capacity.

P_{50} is the O_2 tension at which Hb is 50 % saturated. It is normally = 26.8 mmHg (3.58 kPa).

The normal curve shows:

- At alveolar O_2 tension (PAO_2) **100 mmHg**; PaO_2 is **> 90 mmHg** (about 95 mmHg) and SaO_2 is nearly **100** % (about 97.5 %) and becomes almost independent of PaO_2. This ensures adequate O_2 supply to the tissues.
- At PaO_2 **70 mmHg**; SaO_2 is **93%** i.e., PaO_2 can decrease by about 1/3 (as occurs in high altitudes and some pulmonary diseases) without a large decrease in SaO_2 %.

N.B.: Venous oxygen saturation is typically 74% which corresponds to a PO_2 of 40 mmHg (5.33 kPa).

- At PaO_2 **60 mmHg**; SaO_2 is **90%.**
- At PaO_2 **40 mmHg** (that of venous blood); SaO_2 is **75%** i.e., arterial Hb is about 25% desaturated.

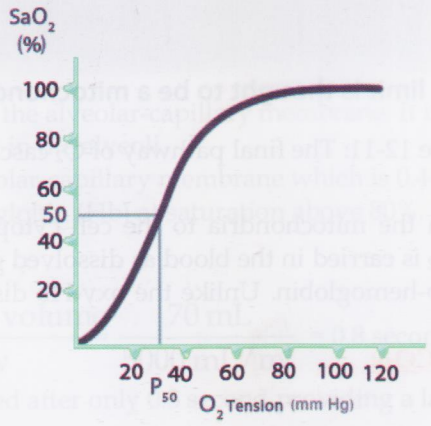


Figure 12-12: Hb-dissociation curve

• At PaO_2 **40 to 20 mmHg**; the curve is steep (vertical) where a slight decrease in PaO_2 is associated with a marked decrease in % saturation (thus supplying more O_2 to tissues). This is important in muscle exercise as PaO_2 in active muscles decreases sharply causing more O_2 diffusion from the blood. Therefore, when PaO_2 is decreased, increased desaturation of Hb occurs and consequently more release of O_2 to active muscles occurs (about 3 times as much as during rest).

Factors Affecting the O_2-Hb Dissociation Curve:

Factors that shift the curve to left i.e., there is increased affinity of Hb to O_2; so, less O_2 is delivered and a lower P_{50} is produced.	**Factors that shift the curve to right** i.e., there is decreased affinity of Hb to O_2; so, more O_2 is delivered and a higher P_{50} is produced.
1. Decreased H^+ concentration (i.e., increased pH or alkalinity). 2. Decreased $PaCO_2$. 3. Decreased temperature. 4. Decreased concentration of 2, 3 DPG (Di-phosphoglycerate) in red blood cells as in: • Increased $[H^+]$. • Old age red blood cells as in old stored blood. • Fetal blood (HbF). 5. Decreased Hb concentration as anemia or hemolysis. 6. Abnormal Hb as carboxy-Hb (carbon monoxide poisoning), met-Hb, cyanide, fetal Hb and sickle Hb.	1. Increased H^+ concentration (i.e., decreased pH or acidity). 2. Increased $PaCO_2$. 3. Increased temperature 4. Increased concentration of 2, 3 DPG (Di-phosphoglycerate) in red blood cells as: • Decreased $[H^+]$. • Newly formed red blood cells as in chronic hypoxia as in high altitudes and exercise. • Pregnancy. 5. Increased Hb concentration as in polycythemia and pregnancy. 6. Drugs as cortisol, aldosterone, and methylprednisolone.

N.B.: The Bohr Effect:

It is the normal difference between pH and PCO_2 in arterial and venous blood which equals 0.04 and 0.8 kPa (6 mmHg) respectively. This difference decreases the affinity of hemoglobin to oxygen, and shifts the oxy-hemoglobin dissociation curve approximately 5% to the right.

Control of Breathing

Respiratory Centers:

There are 2 centers in the medulla:

1- **A dorsal respiratory group**: primarily active during **inspiration.**

2- **A ventral respiratory group**: primarily active during **expiration** (figure 12-13).

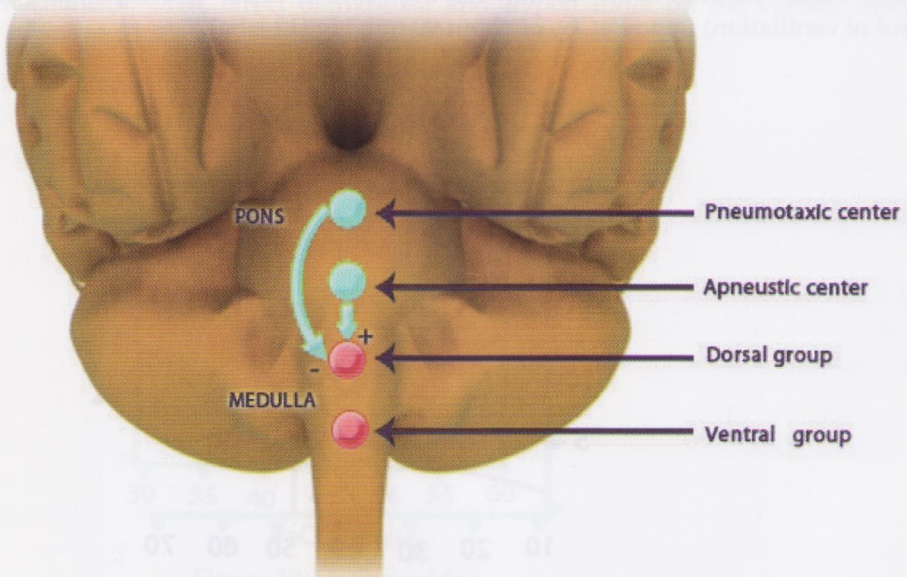


Figure 12-13: Respiratory centers

• The origin of the basic rhythm is due to either: (not firmly established)
- Intrinsic spontaneous discharge activity in the dorsal group
or - Reciprocating activity between the dorsal and ventral groups.
• Just dorsal to the ventral respiratory group is a region called the **pre-Bötzinger complex cells** which seems to be able to generate a pacemaker activity related to voltage-dependent ion channels (much like cardiac pacemaker cells), but it is not clear whether these cells can initiate respiratory rhythm alone or with the help of the dorsal and ventral respiratory groups.

• There are 2 pontine areas influencing the dorsal (inspiratory) medullary center:
1- A **lower pontine (apneustic)** center which is **excitatory**.
2- An **upper pontine (pneumotaxic)** center which is **inhibitory.**
Both pontine centers appear to fine-tune the respiratory rate and rhythm as a lesion of the brain-stem below the pontine centers causes a medullary gasping pattern of respiration suggesting that the rhythm is generated in the medulla and fine tuned in the pons.
• Respiratory center balances the depth of respiration (tidal volume) against the rate to spend the least energy of breathing as:
- Increased elastic work of breathing (e.g., pulmonary edema or fibrosis) increases the respiratory rate.
- Increased resistive work of breathing (e.g., asthma) increases the depth of breathing (Vt).

Respiratory Center is affected by:

I- Central Sensors:

1- Central Chemoreceptors:

They lie on the antero-lateral surface of the **medulla** (floor of the 4th ventricle) near the ventral respiratory group.
They respond to changes in cerebrospinal fluid (CSF) H^+ concentration.

$$CO_2 + H_2O \leftrightarrow H^+ + HCO_3^-$$

As the blood brain barrier is permeable to dissolved CO_2, but not to HCO_3^- ions, acute changes in $PaCO_2$ are reflected in CSF H^+ concentration. Increased $PaCO_2$ causes increased CSF H^+ concentration which in turn activates central chemo-receptors. This increases alveolar ventilation which reduces $PaCO_2$ back to normal. The reverse also occurs (this is a rapid response) i.e., central chemoreceptors are affected by $PaCO_2$ and not pH of the blood.

2- Higher Centers in the Brain Including the Cerebral Cortex

as the pattern of respiration is modulated by speech, ingestion of food and drink, and anticipation of exercise.

The Relation between $PaCO_2$ and Alveolar Ventilation (Minute Ventilation):

A) In an Awake Subject, Curve "A":

It is formed of 2 parts (figure 12-14):
• When $PaCO_2$ exceeds about **46 mm Hg** the curve is linear (corresponding to involuntary medullary control of ventilation) up to $PaCO_2$ of about 90 mm Hg (12 KPa).

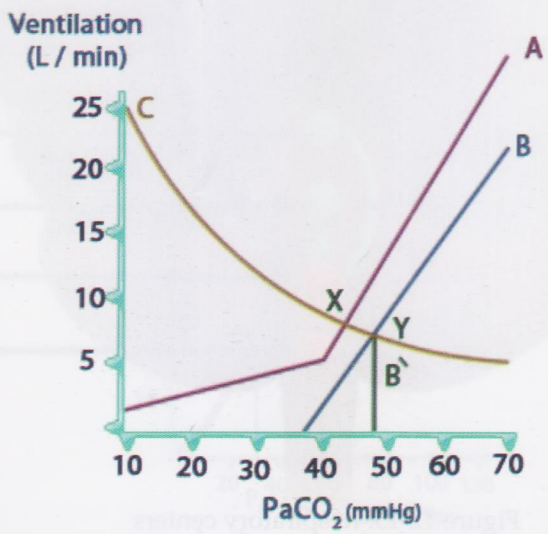


Figure 12-14: The relation between $PaCO_2$ and minute ventilation

N.B.: Very high $PaCO_2$ depresses the ventilatory response (i.e., CO_2 narcosis).

• **Below 46 mm Hg,** the curve takes **a hockey stick appearance** due to the effect of consciousness (cerebral cortex) on respiratory control i.e., awake drive to breath. Therefore, apnea does not occur.

B) In Spontaneously Breathing Anesthetized Patient, Curve "B":

• Slight decrease in $PaCO_2$ (from manual hyperventilation) may completely abolish spontaneous ventilatory efforts i.e., the tail or the hockey stick appearance of curve "A". The transection of curve "B" with the abscissa is the **apneic threshold,** below which spontaneous ventilation ceases.

• There is a **hysteresis effect**; as once the ventilatory drive is abolished by hyperventilation, it is necessary for $PaCO_2$ to increase several mm Hg (4-5 mm Hg) above the apneic threshold before spontaneous ventilation resumes (line B-).

C) CO_2 Excretion Hyperbola, Curve "C":

• This is a graphical representation of the CO_2 wash (i.e., decreased $PaCO_2$) when alveolar ventilation increases.

• The exact position of the hyperbola depends upon CO_2 production and barometric water vapor pressure.

• The interaction of the ventilatory response curves (of awake and anesthetized patient) and the CO_2 excretion hyperbola i.e., X and Y points determine steady-state alveolar ventilation and $PaCO_2$.

II- Peripheral Sensors:

1- Peripheral Chemoreceptors:

• They lie in - carotid bodies (at the bifurcation of the common carotid arteries). They are the main ones.
- aortic bodies (surrounding the aortic arch). They have no significant role.

• They are stimulated by - decreased PaO_2 (mainly).
- increased $PaCO_2$.
- increased H^+ concentration i.e., low pH.
- decreased arterial perfusion pressure.

Also they are stimulated by cyanide, doxapram, and large doses of nicotine.

The impulses are transmitted through the glosso-pharyngeal nerve to stimulate the respiratory center, which in turn increases alveolar ventilation.

• The receptor activity increases markedly when PaO_2 decreases to less than 50 mm Hg.

• Cells of the carotid body (glomus cells) are thought to be the primarily dopaminergic neurons; so, anti-dopaminergic drugs (as phenothiazines), most commonly used anesthetics, and bilateral carotid surgery can abolish the peripheral ventilatory response to hypoxia.

As O_2 saturation decreases, the slope of the ventilatory response to CO_2 increases, producing a family of CO_2 response curves (the so-called "**Oxford Fan**" (figure 12-15).

Therefore, on measuring hypercarbic ventilatory response, it is necessary to maintain a constant degree of hypoxic stimulation. This is usually achieved by using high inspired O_2 concentrations, effectively turning off the hypoxic drive mechanism. The effect of hypoxia and hypercapnia on the carotid bodies is synergistic.

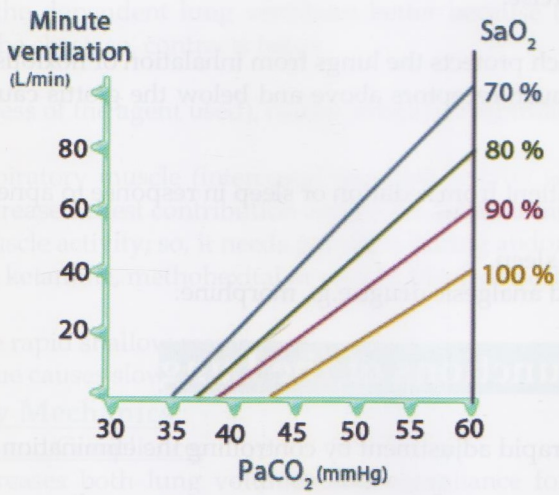


Figure 12-15: Oxford fan

N.B.: Disorders of Ventilatory Control:

1- Neonates of low postconceptual age (< 60 weeks) have apneic spills and sudden infant death syndrome may occur due to immaturity of ventilatory control systems.

2- Ondine's curse: originally described after surgery near the upper cervical spinal cord, resulting in profound hypoventilation during sleep or anesthesia due to abnormalities in the cervical integratory system that blunts the hypoxic and hypercapnic ventilatory responses.

3- Idiopathic varieties of Ondine's curse are found in children and are referred to as primary central alveolar hypoventilation syndromes.

4- Morbidly obese patients have sleep apnea syndrome due to abnormalities in ventilatory control.

5- Drug induced sedation.

2- Lung Receptors:

a- Stretch Receptors: (via the vagus nerve)

They are present in smooth muscles of the airways. They are responsible for inhibition of inspiration when the lung is inflated to excessive volumes (**Hering-Breuer inflation reflex**) and shortening of expiration when the lung is deflated (**Deflation reflex**).

N.B.: **Head's paradoxical reflex:** (by the vagus nerve also)

It occurs when an anesthetized patient completes a breath which is initiated by compressing the reservoir bag. It is paradoxical because unlike the Hering-Breuer reflex, pulmonary expansion causes further inhalation rather than initiating exhalation.

b- Irritant Receptors:

They are in the tracheo-bronchial mucosa. They are stimulated by noxious gases, smoke, dust and cold gases causing a reflex increase in respiratory rate, broncho-constriction and coughing.

c- "J" Receptors (Juxta-Capillary Receptors):

They are in the interstitial space within alveolar walls. They are stimulated by expansion of interstitial space volume and by various chemical mediators following tissue damage causing dyspnea.

N.B.: **Cough**

Definition: maximal inspiration followed by a forced expiration against a closed glottis during which intra-thoracic pressure may reach 80 cm H_2O. Then the larynx opens allowing expiration to occur at maximum velocity. It may occur voluntarily or as a reflex.

The increased intra-thoracic pressure causes dynamic compression of bronchi which causes:

- Further increase in the velocity of expired air approaching the speed of sound.
- Creating shear forces which detach the mucus from the mucosa and sweeps it from smaller to larger bronchi.

Effective cough requires - an adequate inspiratory volume.
- an adequate expiratory power.
- a functioning glottis.

3- Other Receptors:

1- Various Muscle and Joint Receptors:

They are important during exercise.

2- Laryngospasm:

It is a very primitive reflex which protects the lungs from inhalation of noxious substances.

Stimulation of chemical and touch receptors above and below the glottis causes laryngospasm. It is less vigorous in the elderly.

3- Arousal Response:

It is the ability to arouse the patient from sedation or sleep in response to apnea, airway obstruction or the need to cough.

It is obtunded - during normal sleep.
- by sedative and analgesic drugs e.g., morphine.

Non-Respiratory Functions of the Lung

1- Acid-Base Balance:

The respiratory system makes rapid adjustment by controlling the elimination of CO_2.

2- Metabolic Function:

a- Synthesis:

1- **Surfactant**: see before.

2- **Coagulation factors including heparin.**
3- O_2-derived free radicals are produced by neutrophils and macrophages in the lung in response to infection (**superoxide radicals**).
4- **Histamine** synthesis and release during allergic reactions.
b- Metabolism:
1- Conversion of angiotensin I (inactive) to angiotensin II (active) by **angiotensin converting enzyme** which is bound on the surface of the pulmonary endothelium.
2- Pulmonary endothelium **inactivates norepinephrine, serotonin, bradykinin, prostaglandins and leukotrienes.**

3- Filtration Function:

• The unique in-series position of the pulmonary capillaries allows them to act as a filter for debris in the blood-stream (e.g., thrombi).
The theoretical pore size of the lung as a filter is about 70 μm, although in practice much larger particles can traverse the lungs via arterio-venous connections.
• Active proteolytic system, plasmin activators, heparin, and thromboplastin facilitate breakdown of entrapped fibrin debris.

4- Pulmonary Defense Mechanisms:

1- The nose and the tracheo-bronchial tree:
They are lined by mucus-secreting ciliated epithelium. Cilia sweep the mucus coat with the entrapped particles to the pharynx.
2- Cough.
3- Pulmonary macrophages:
They phagocytose inhaled particles and produce proteases and O_2 free radicals (superoxide radicals) to kill the bacteria.
N.B.: Lungs contain α_1 anti-trypsin to inactivate the proteases and contain superoxide dismutase to inactivate superoxide radicals to prevent damaging themselves.
4- Immunoglobulin A (IgA):
It is secreted in pulmonary mucus and contributes to killing micro-organisms.

Effect of Anesthesia on Respiration

1- Effect on the Cell Metabolism:

General anesthesia decreases both $\dot{V}CO_2$ and $\dot{V}O_2$ by 15% especially cerebral and cardiac consumption. Hypothermia decreases them too.

2- Effect on Respiratory Pattern:

1- Position:
• In the supine position, abdominal breathing predominates as the diaphragm becoming at a higher position in the chest (about 4 cm), allows it to contract more effectively than when the patient is upright.
• In the lateral position, the dependent lung ventilates better because the dependent hemi-diaphragm takes a higher position in the chest; so, contracts better.
2- Depth of Anesthesia:
• Light anesthesia (regardless of the agent used), causes irregular respiration, and breath-holding.
• Induction of anesthesia:
- It decreases thoracic inspiratory muscle (intercostal muscles) activity with relative preservation of the diaphragm; so, there is decreased chest contribution and increased abdominal contribution.
- It increases expiratory muscle activity; so, it needs paralysis during abdominal surgery.
This is not prominent with ketamine, methohexital or up to 1 MAC of isoflurane.
3- Agent Used:
• Inhalational agents cause rapid shallow respiration.
• Nitrous-narcotic technique causes slow deep respiration.

3-Effect on Pulmonary Mechanics:

1- Effect on Lung Volumes and Compliance:
• General anesthesia decreases both lung volumes and compliance for example, Functional residual capacity (FRC) decreases about 15-20% (400-500 mL) up to 40% in some patients. It is not related to

anesthesia depth as it may persist for several hours after anesthesia. Trendelenburg position (> 30 degrees) causes further decrease in FRC as intra-thoracic blood volume increases. General anesthesia in sitting position produces little effect on FRC, while muscle relaxants have no effect on FRC.

2- Effect on Airway Resistance:

• General anesthesia decreases FRC; so, it increases airway resistance which is not usually observed due to broncho-dilating properties of volatile inhalational anesthetics.

3- Effect on Work of Breathing:

• General anesthesia increases work of breathing due to:

- Decreased chest and lung compliance.
- Increased airway resistance.

4- Effect on Ventilation/Perfusion Matching:

1- The Distribution of Perfusion:

• General anesthesia has no effect on perfusion during spontaneous respiration, but increased intra-thoracic pressure of mechanical ventilation may decrease cardiac output, increasing or creating lung zone in which PA > Pa > Pv. Therefore, there is an increase in dead space.

2- The Distribution of Ventilation:

• General anesthesia causes impaired ventilation during spontaneous respiration which is worsened during mechanical ventilation as there is reduction of ventilation to the dependent parts of the lungs. This causes atelectasis in dependent parts of the lung.

3- Hypoxic Pulmonary Vasoconstrictive Reflex:

• It is abolished by the low concentration of volatile agents; therefore, the net effect of anesthesia is increased both dead space and shunt in anesthetized patient. This increases $PaCO_2$ and decreases PaO_2. It is conventional to administer a gas mixture with FiO_2 of about 0.3 during general anesthesia at least.

5- Effect on Gas Exchange and Carriage:

• General anesthesia causes:

- impairment of gas exchange due to ventilation/perfusion mismatching.
- decreased cardiac output which decreases O_2 carriage, but the decreased metabolic rate tends to compensate for the decreased O_2 delivery.
- hyperventilation which decreases $PaCO_2$. It in turn shifts O_2-Hb curve to the left causing decreased O_2 delivery.
- postoperative shivering which increases O_2 consumption.

• Secondary gas effect of N_2O causes hypoxia postoperatively.

6- Effect on Control of Breathing:

a- Narcotics:

• In awake patients, narcotics shift the CO_2 response curve to the right, while in sedated or anesthetized patients, they decrease the slope of the response (by about 70%) which is more risky, up to apnea. This is reversed by naloxone.

b- Induction Agents:

• Thiopental decreases the slope (by 25-30%) which returns to normal within 5 min after injection i.e., before the patient regains his consciousness (it is manifested as a period of apnea).

• Propofol decreases the slope (by 50%) which returns to normal within 20 min after injection i.e., after the patient regains his consciousness. It depresses the central chemo-receptors mainly with minimal effect on the peripheral chemo-receptors.

c- Midazolam:

• Oral route has a minimal effect.

• I.v. route has a greater effect (especially if with opioids). It is reversed by flumazenil.

d- Inhalational Agents:

• They depress the peripheral chemoreceptors more than the central chemoreceptors. In patients with chronic obstructive airway diseases, the central chemoreceptors are depressed by a chronic increase in $PaCO_2$; so, they depend on peripheral chemo-receptors (hypoxic drive). Thus, they are at risk of respiratory depression due to effect of the residual concentration of inhaled anesthetics which depress peripheral chemoreceptors.

Anesthesia with Respiratory Diseases

Preoperative Patient Evaluation

1- Preoperative Detection of Pulmonary Risk Factors, which can predict the possibility of **postoperative pulmonary complications**.

Predisposing Factors of Postoperative Pulmonary Complications: should be detected preoperatively.

a- Patient Specific:

1- Preexisting pulmonary disease: such as chronic obstructive pulmonary diseases (COPD)
Patients suffer from pulmonary symptoms such as:

- Dyspnea and its relation to exertion.
- Cough (productive or not).
  - Purulent sputum indicates active infection which should be treated preoperatively.
  - Chronic copious sputum indicates bronchiectasis or lung abscess.
- Wheezes indicate the degree of obstructive lung disease.
- Hemoptysis.
- Chest pain.

These preexisting pulmonary diseases should be treated aggressively before surgery to decrease postoperative pulmonary complications.

2- Smoking: is discussed in details in chapter "The Practice Conduct of Anesthesia".

3- Obesity (morbid obesity): decreases functional residual capacity (FRC) and increases the work of breathing and the risk of deep venous thrombosis.

4- Age > 60 years.

5- Other risk factors such as alcohol use, myocardial infarction, renal failure, blood transfusion, and impaired sensorium can precipitate postoperative pulmonary complications.

b- Surgery Specific:

1- Prolonged **general anesthesia and surgery > 3 hours.**

2- **Site of incision:**

Thoracic incisions > upper abdominal incisions > lower abdominal incisions and vertical incisions > transverse incisions are associated with more reduction of **the vital capacity (40%) and FRC (40-60%) than other incisions**; this effect is maximal in the 1st postoperative day and usually lasts for 5-10 days (up to 14 days) postoperatively.

3- **Emergency surgery**.

The anesthetic technique has a little effect on the incidence of postoperative pulmonary complications.

Respiratory Risk Index Score

It is used to predict the probability of postoperative respiratory complications and failure.

Variables	Point Value
• Type of surgery:	
- Abdominal aortic aneurysm	27
- Thoracic surgery	21
- Neurosurgery, upper abdominal or peripheral vascular surgeries	14
- Neck	11
• Emergency surgery	11
• Albumin < 3 g/dL	9
• Blood urea nitrogen > 30 mg/dL	8
• Partially or fully dependent status	7
• History of COPD	6
• Age in years - ≥ 70	6
- 60-69	4

Class	Total Points	% of Respiratory Complications or Failure
1	≤ 10	0.5%
2	11-19	1.8%
3	20-27	4.2%
4	28-40	10.1%
5	> 40	26.6%

2- Detect the Presence of Complications e.g., corpulmonale.

3- History of Drug Intake and their Complications as:

- Steroids: Perioperative cover should be given.
- Bronchodilators: They should be continued up to the time of surgery.
- Digoxin, diuretics: in patients with corpulmonale.

4- Preoperative Assessment of Other Systems such as cardiovascular system.

Preoperative Investigations

1. Chest X-ay:

- It is a poor indicator of functional impairment. The American Society of Anesthesiologists (ASA) has stated that chest radiographs are not indicated on the basis of age or preexisting respiratory condition unless there is a surgical indication or a need to establish the presence or absence of a defined pulmonary condition.
- Chest x-ray may be important in the following conditions:

  1- As a baseline for assessing postoperative radiographs.

  2- To detect any localized disease of the lungs and pleura not detected on clinical examination e.g., neoplasm, bullae, collapse, consolidation and effusion.

  3- To detect any generalized disease of the lungs in patients with acute pulmonary symptoms e.g., pulmonary fibrosis, emphysema, and pneumothorax.

  (N.B.: Picture of emphysema; hyperlucency, flattening of the diaphragm, vertically oriented cardiac shadow, and bullae) (figure 12-16).

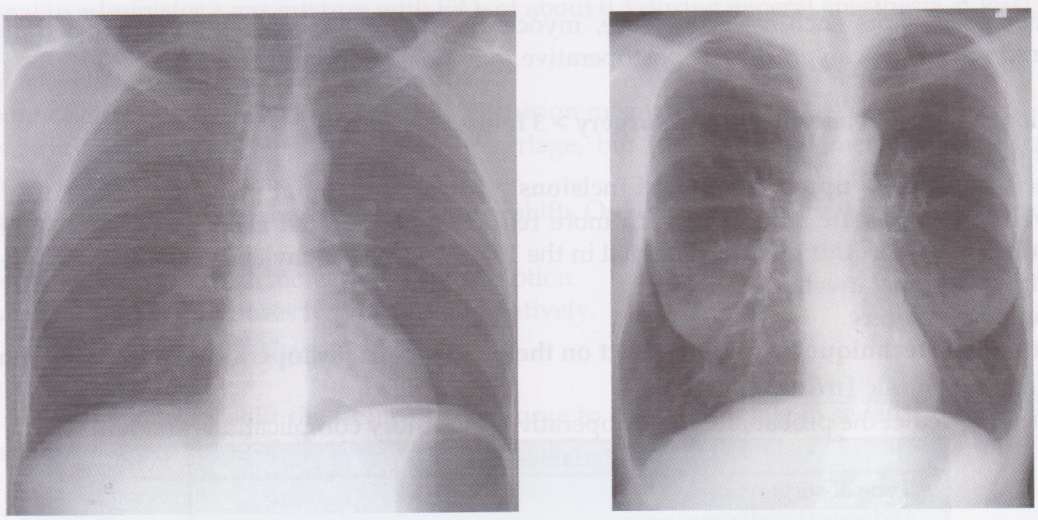


Figure 12-16: Two plain chest x-rays; normal (left) and emphysema (right)

2. Electrocardiogram (ECG):

It may show - right ventricular hypertrophy or strain i.e., corpulmonale.
or - ischemic heart diseases.

3. Hematology: may show

- Polycythemia: due to chronic hypoxemia.
- Anemia: this increases tissue hypoxia.
- Leukocytosis: ▫ Neutrophilia: due to active bacterial infections.
  ▫ Lymphocytosis: due to viral infection.
  ▫ Eosinophilia: The count of eosinophils parallels the degree of airway inflammation and hyper-reactivity in asthma; so, it can be used to assess the degree of asthma.

4. Sputum Examination:

Culture and sensitivity test is done for patients with acute infections or chronic lung diseases.
It contains eosinophils in bronchial asthma or neutrophils in bronchitis or pneumonia.

5. Computed Tomography (CT). (figure 12-17)

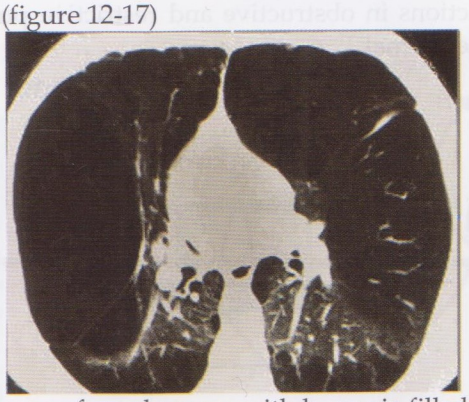


Figure 12-17: CT scan of emphysema with large air-filled bullae; note that only the narrow anterior junction line separates the two lungs at the front

6. Magnetic Resonance Imaging (MRI).

7. Radioisotope Scan: to assess regional lung function. It is important before lung resection. The overall lung function is unlikely to be significantly impaired if the resectable area has poor function.

8. Arterial Blood Gas Measurement:

Indications:
- Suspected acute hypoxemia.
- Chronic lung disease undergoing significant surgery.
- Marked abnormal pulmonary function tests.

Values:

1. Increased $PaCO_2$ > 45 mm Hg is a strong prognostic indicator of postoperative pulmonary complications (if $PaCO_2$ is ≥ 50 mm Hg, it indicates the increased need for postoperative ventilation).
2. Decreased PaO_2 and dyspnea at rest indicate the increased need for postoperative ventilation.

9. Pulmonary Function Tests:

They can differentiate between obstructive and restrictive lung diseases.
If they are less than 50 % of the predicted, postoperative ventilation is needed.

Pulmonary Function Tests	Obstructive	Restrictive
1) - Forced expiratory volume in 1 sec (FEV1): normally > 80% of FVC - Forced vital capacity (FVC). - FEV1/FVC ratio	- ↓↓ due to ↑ airway resistance - little effect - ↓ (< 75% predicted)	- ↓ due to normal airway resistance - ↓↓ due to ↓ expansion of the lung and chest wall. - Normal or ↑
2)- Vital capacity (VC)	- Normal / or ↓	- ↓
3)-Total lung capacity (TLC) - Residual volume (RV) - Functional residual capacity (FRC)	- ↑ - ↑ - ↑ i.e., there is air trapping	- ↓ - ↓ - ↓ i.e., there is no air trapping
4) Maximum mid-expiratory flow rate (MMEFR) (= Forced Expiratory Flow or FEF 25-75%). It is obtained by dividing the volume between 25-75% of VC by the corresponding elapsed time. This is the only abnormality present early in the course of the disease. 5) Maximum breathing capacity (MBC) Normally = > 125 L/min 6) Peak Expiratory Flow Rate (PEFR): is the greatest flow velocity that can be obtained during forced exhalation, starting with lungs fully inflated.	- ↓ - ↓ - ↓	- N - N - N
7)-Total compliance - Airway resistance - The work of breathing	- N - ↑ - ↑	- ↓ - N - ↑

N = normal ↓ = decreased ↑ = increased

The changes in pulmonary functions in obstructive and restrictive pulmonary diseases are apparent in figure 12-18 in comparison to the normal.

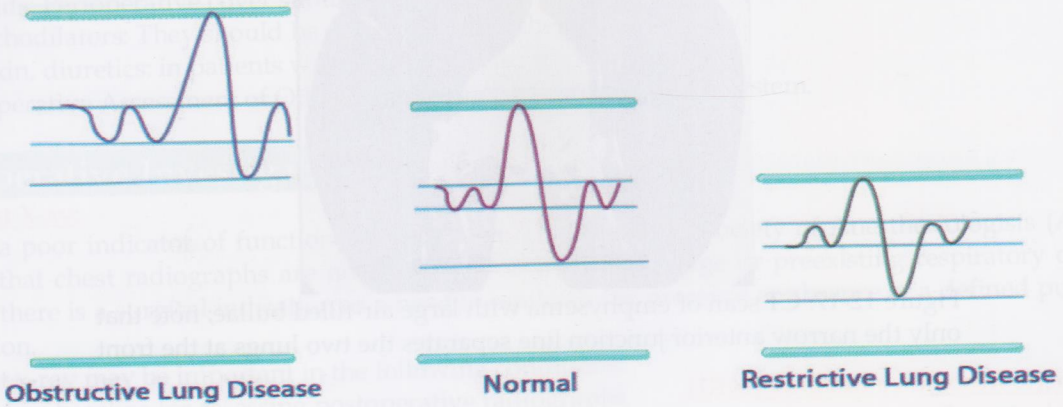


Figure 12-18: Pulmonary function tests in obstructive lung diseases (left), normal (middle), and restrictive lung diseases (right)

10. Flow-Volume Loops:

They provide a graphic analysis of flow at various lung volumes.

The normal curve (figure 12-19) is discussed in details in chapter "Monitoring for Anesthesia & Intensive Care".

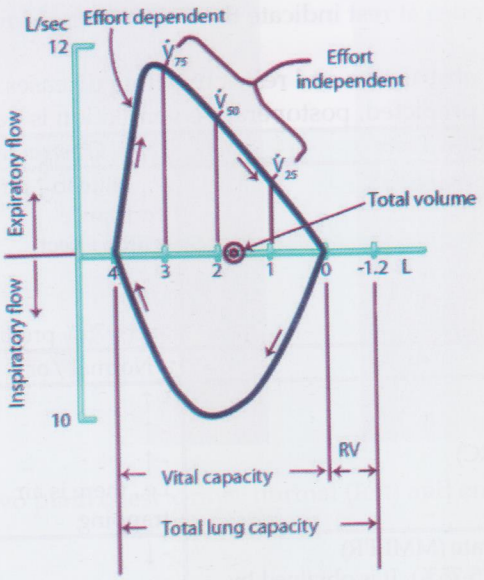


Figure 12-19: Flow-volume loops

The Shape of the Loop is Specific for Each Disease: (figure 12-20)

Normally; the ratio of expiratory flow to inspiratory flow at 50% of the VC (mid-VC flow ratio) is about 1.0

	Obstructive Lung Disease	Restrictive Lung Disease
FEV_1	- ↓↓	- ↓ or little effect
FVC	- Normal or little effect	- ↓↓
TLC	- ↑	- ↓↓
$FEF_{25-75\%}$ & Mid-VC flow ratio	- ↓ - ↓	- Normal - Normal
Shift of the loop	- To the left with downward scooping of the expiratory limb	- To the right

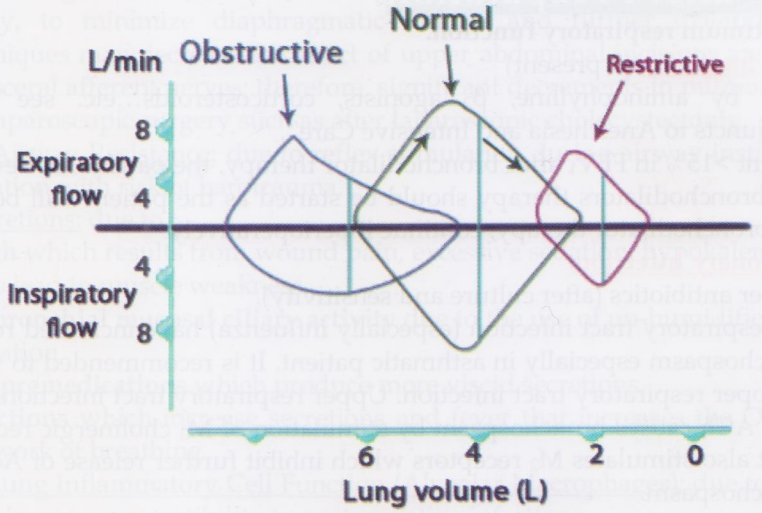
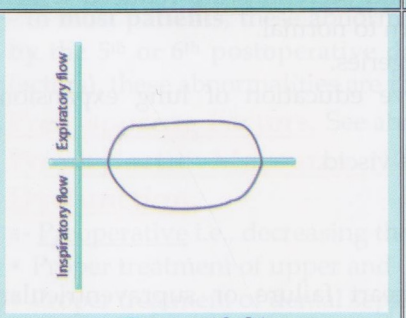
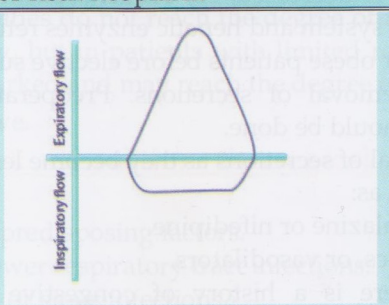
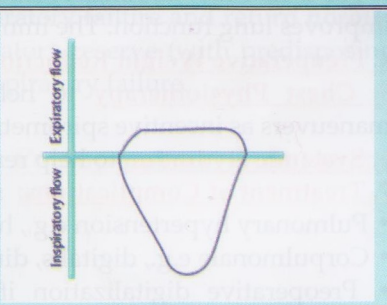


Figure 12-20: Flow-volume loops in different diseases

The cause of airway obstruction can be identified (figure 12-21, 22, and 23).

Fixed Obstruction (Intra-or Extra-Thoracic) e.g., tracheal stenosis, tumors or goiters.	**Variable Extra-Thoracic Obstruction** e.g., vocal cord paralysis, vocal cord neoplasm, or neck neoplasm	**Variable Intra-Thoracic Obstruction** e.g., tracheomalacia or bronchial tumors
 Figure 12-21	 Figure 12-22	 Figure 12-23
- **Plateau** occurs in **both** the inspiratory and expiratory cycles.	- **Plateau** occurs in the **inspiratory** cycle because during inspiration, the negative intra-thoracic pressure pulls the extra-thoracic airway causing collapse of the airway. - Expiratory flow is nearly normal or minimally decreased because the positive pressure inside the airway decreases the obstruction.	- The inspiratory flow is nearly normal or minimally decreased because the negative intra-pleural pressure (intra-thoracic pressure) increases the diameter of the airway (it acts as a stent to the airway). - **Plateau** occurs in the **expiratory** flow because the positive intra-thoracic pressure decreases airway diameter causing decreased expiratory flow.

N.B.: Variable obstruction means a lesion whose influence varies with the phase of respiration.

Q: Discuss different airway graphs and their clinical applications?

A: 1- Flow volume loops.

2- Static pulmonary function tests.

3- Lung compliance curve.

4- Capnography.

5- Different ventilator mode graphs.

Preoperative Patient Preparation

Aim: To reach the optimum respiratory function.

1. Treatment of Bronchospasm: (if present)

It is best achieved by aminophylline, β_2 agonists, corticosteroids...etc. see before chapter of "Pharmacological Adjuncts to Anesthesia and Intensive Care".

If there is improvement >15% in FEV_1 after bronchodilator therapy, the patient has reversible obstruction; therefore, long term bronchodilators therapy should be started as the patient will benefit from it. If the patient is already on bronchodilator therapy, continue it perioperatively.

2. Treatment of Pulmonary Infection:

It is achieved by proper antibiotics (after culture and sensitivity).

Patients with upper respiratory tract infection (especially influenza) have increased reactivity of airways, which increases bronchospasm especially in asthmatic patient. It is recommended to wait 2-3 weeks after clinical recovery of upper respiratory tract infection. Upper respiratory tract infections cause alteration in M_2 receptor function. ACh causes bronchospasm by stimulation of M_3 cholinergic receptors on bronchial smooth muscle, but it also stimulates M_2 receptors which inhibit further release of Ach. Alteration of M_2 receptors causes bronchospasm.

3. Stop Smoking is very important. Cessation of smoking for:

- **At least 12 hours**: Carboxy-Hb (carry carbon monoxide) is decreased. Its half life is 4-6 hours. This increases O_2 carrying capacity.
- **At least 2 days**: The stimulant effect of nicotine on cardiovascular system is abolished and the improvement of the ciliary function occurs.
- **1-2 weeks**: Sputum volume is decreased.
- **For 2 months**: Chronic bronchitis is decreased; so, bronchospasm and secretions are reduced which improves lung function. The immune system and hepatic enzymes return to normal.

4. Preoperative Weight Reduction for obese patients before elective surgeries.

5. Chest Physiotherapy to help removal of secretions. Preoperative education of lung expansion maneuvers as incentive spirometry should be done.

6. Systemic Hydration to help removal of secretions as they become less viscid.

7. Treatment of Complications: such as:

- Pulmonary hypertension e.g., hydralazine or nifedipine.
- Corpulmonale e.g., digitalis, diuretics, or vasodilators.
- Preoperative digitalization if there is a history of congestive heart failure or supraventricular tachycardia.

Postoperative Respiratory Complications and Failure

Definition:

It is occurrence of **hypoxia and hypercapnia** with **possibility of failure of extubation** 48 hours after surgery.

Incidence:

- after thoracic and upper abdominal surgeries: 20-40%.
- after lower abdominal surgery (2-5%).

Causes and Mechanisms:

Respiratory impairment occurs especially after abdominal and thoracic surgery due to:

1- Reduction of Functional Residual Capacity Postoperatively: due to:

- Anesthetic agents, especially **inhalational anesthetics,** that produce:
  - **Uncoordination of respiratory muscles** (diaphragm and accessory muscles). This uncoordinated activity reduces efficiency and **causes hypoventilation**.
  - **Changes in the shape of the chest,** which in turn decrease the lung functions and produce **atelectasis** in dependent lung regions. This causes **ventilation/perfusion mismatching**.
- **Postoperative abdominal distension** that may cause diaphragmatic splinting.
- **Postoperative supine position**.
- **Postoperative wound pain** that causes spasm of expiratory muscles and voluntary limitation of their motion to minimize postoperative pain.
- **Thoracic or abdominal surgical incisions** that produce disruption of respiratory muscles (e.g., abdominal or intercostal muscles) which will not function normally in the initial stages of healing.
- **Stimulation of visceral afferent nerves** markedly changes the activation of respiratory muscles.

N.B.: Removal of the gall bladder activates vagal afferents, which produces a reflex inhibition of diaphragm activity, to minimize diaphragmatic motion and further irritation of these afferents. Laparoscopic techniques may decrease the effect of upper abdominal incisions and the wound pain, but not the effect of visceral afferent nerves; therefore, significant decrements in pulmonary function may still be observed after laparoscopic surgery such as after laparoscopic cholecystectomy.

2- An Increase in Airway Resistance: due to reflex stimulation during airway instrumentation. This may produce hyperinflation with risk of barotrauma.

3- Retention of Secretions: due to

- **Inability to cough** which results from wound pain, excessive sedation, hypokalemia or hypophosphatemia. These factors lead to muscle weakness.
- **Suppression of bronchial mucosal ciliary activity** due to the use of un-humidified anesthetic gases and endotracheal intubation.
- **Anti-sialagogue premedications** which produce more viscid secretions.
- **Pulmonary infections** which increase secretions and fever that increases the O_2 consumption that in turn increases the work of breathing.

4- Impairment of Lung Inflammatory Cell Function (Alveolar Macrophages): due to prolonged anesthesia and surgery which increase susceptibility to postoperative infections.

- All these mechanisms cause an increase in respiratory rate, a decrease in tidal volume, a decrease in functional residual capacity and vital capacity, and an abnormal pattern of chest wall motion. These finally lead to **atelectasis** (usually small and not visible radiologically) and **pulmonary infection** (which causes pneumonia).
- Finally hypoxia and hypercapnia occur with an increase in the work of breathing and muscle fatigue resulting in **respiratory failure**.
- In **most patients**, these abnormalities do not reach the degree of respiratory failure and return **normal by the 5th or 6th postoperative day,** but in patients with limited respiratory reserve (with predisposing factors), these abnormalities are marked and may reach the degree of respiratory failure.

Predisposing Factors: See above.

Prophylactic Measures (Risk Reduction Strategies) for Postoperative Pulmonary Dysfunction:

a- Preoperative i.e., decreasing the predisposing factors.

- Proper treatment of upper and lower respiratory tract infections.
- Proper treatment of dental sepsis or sinus infections.
- Reaching the optimum condition for chronic respiratory diseases such as proper treatment of chronic obstructive airway disease.
- Encouraging cessation of smoking for at least 6 weeks.
- Decreasing body weight.
- Initiating patient education regarding lung volume expansion maneuvers.
- Avoid heavy premedications in patients with risk factors.

b- Intraoperative:

- **Some physicians prefer and recommend regional anesthesia**, but;
  - It may block the respiratory accessory muscles causing more respiratory impairment.
  - Sedation, given during regional techniques, may affect respiratory function.
- **General anesthesia can be used**, but with the following precautions:
  - Sterile equipment and tubes should be used to avoid introduction of infection.
  - Humidified gases should be administered during prolonged procedures.
  - Adequate reversal of neuromuscular blocking agents should be achieved.
- Use **minimally invasive surgery (endoscopic) techniques** when possible.
- Avoid surgical procedures likely to require more than 3 hours.

c- Postoperative:

- Proper postoperative analgesia such as neuraxial opioids, intercostal nerve blocks, and patient-controlled analgesia.
- Proper physiotherapy.
- Instituting lung volume expansion maneuvers (voluntary deep breathing, incentive spirometry, continuous positive airway pressure e.g., 7.5 cm H_2O).

Pulmonary diseases include:

- Obstructive pulmonary diseases.
- Restrictive pulmonary diseases.
- Pulmonary embolism.
- Others as bronchial carcinoma, tuberculosis.

All finally cause respiratory failure.

Obstructive Pulmonary Diseases

They include:

1- Acute Obstructive Pulmonary Disease (Bronchial Asthma).
2- Chronic Obstructive Pulmonary Disease (COPD).
3- Bronchiectasis.
4- Cystic fibrosis.
5- Kartagner syndrome.
6- Bronchiolitis obliterans.
7- Tracheal stenosis.

All these diseases increase airway resistance.

Bronchial Asthma (Acute Obstructive Pulmonary Disease) (Chronic Asthma)

It is episodic, reversible increased airway resistance.

Incidence: 3-5% of population

Types and Pathogenesis: are discussed in figure 12-24.

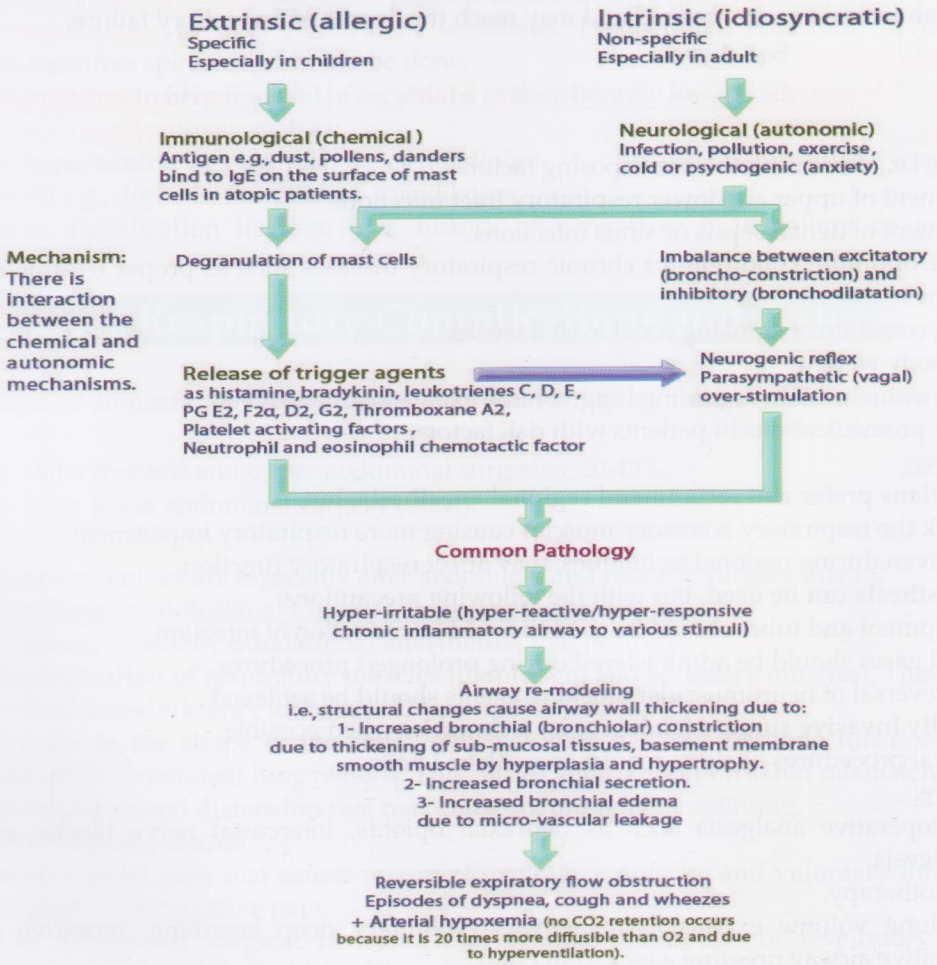


Figure 12-24: Pathogenesis of bronchial asthma

N.B.: **Bronchial asthma** is characterized by **a reversible** increased airway resistance, but **chronic obstructive pulmonary disease (COPD)** is characterized by **irreversible** increased airway resistance. Many patients show mixed pictures. This can be demonstrated by the results of pulmonary function tests before and after bronchodilator. **Increased expiratory airflow, forced expiratory volume in the first second (FEV_1)** after a bronchodilator by 20 minutes **> 15%** is suggestive of a favorable response and indicates bronchial asthma. 10-15% indicates equivocal response.

< 10% indicates poor response which occurs with COPD.

N.B.: **Aspirin-Induced Asthma:** occurs in patients with triad of asthma + nasal polyps + non-steroidal anti-inflammatory drugs (NSAIDs) allergy. NSAIDs inhibit cyclo-oxygenase; therefore, prostaglandin formation from arachidonic acid is decreased and so, arachidonic acid will form leukotrienes which cause bronchospasm.

Preoperative Management:

Preoperative evaluation, preoperative investigations, and **preoperative preparation** are discussed above.

Severity of Bronchial Asthma: can be determined either clinically or by pulmonary function tests:

a- According to the Clinical Condition: Asthmatic patients usually fall into one of 3 groups:

Group I: Patients have a history of asthma, but have been asymptomatic and are on no routine medications.

Group II: Patients with recurrent attacks of asthma, on prophylactic medication, but not actively symptomatic.

Group III: Patients who are symptomatic or who have deteriorated from their normal conditions. In addition to patients who have status asthmaticus.

b- According to Pulmonary Function Tests:

Severity	Expiratory Airflow Obstruction Tests (% of Predicted)			Arterial Blood Gases	
	FEV_1	$FEF_{25\%-75\%}$	PEFR	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)
Mild symptomatic	65-80	60-75	> 70	> 60	< 40
Moderate	50-64	45-59	50-70	> 60	< 45
Severe (Marked)	35-49	30-44	30-49	< 60	> 50
Very severe (status asthmaticus or respiratory failure)	< 35	< 30	< 30	< 60	> 50

The decision to proceed or delay the surgery is taken according to:

A. In elective surgeries:

Surgery can be preceded in patients of group I and II who are not in an attack. If the patient is in an attack or belongs to group III, he or she should be treated first, otherwise the surgery should be postponed.

Treatment of bronchial asthma:

1. Bronchodilators:

- β_2 agonists:
  - Non-selective e.g., epinephrine, or isoprenaline i.v./subcutaneous.
  - Selective e.g., • Fenoterol, or rimiterol aerosol inhaler.
    • Salbutamol, or terbutaline nebulizer, i.v. or oral.
- Methyl-xanthine e.g., aminophylline.

If the patient is **already on aminophylline, its plasma level** should be checked.

- Anticholinergics e.g.,: Ipratropium bromide by metered aerosol.
- Anti-inflammatory: - Hydrocortisone: needs several hours (> 6 hours) to become effective.
  - Cromolyn Na: to prevent a new attack.

B. In emergency surgeries and the patient is in an attack.

Preoperative intensive therapy is needed by O_2, i.v. aminophylline, i.v. or aerosol β_2 agonist and cortisone. The pharmacological details of drugs are discussed in chapter "Pharmacological Adjuncts to anesthesia and intensive care".

Premedications:

1. Sedatives: Oral midazolam 0.5-1 mg/kg is the drug of choice.

2. Anticholinergic agents: e.g., atropine.

Value: • It blocks the vagal reflex-induced bronchospasm.
• It decreases bronchial secretions.

It is especially indicated if - copious secretions are present.
or - ketamine has been used for induction of anesthesia.

Some physicians avoid its routine use because it increases viscosity of secretions and makes them more difficult to clear (only theoretically).

3. Continue treatment:

- Bronchodilators: should be continued up to 1 hour before surgery.
- Cromolyn prophylaxis: should be continued up to the time of surgery.
- Corticosteroids: are given to patients who were receiving long term steroid therapy. Hydrocortisone is given 100 mg pre- and intra- and 6 hours postoperatively, in the 1st day to compensate for adrenal suppression.

N.B.: Avoid H_2 blocking agents (e.g., cimetidine or ranitidine) because:

- H_2 activation causes bronchodilatation while H_1 activation causes bronchoconstriction. Therefore, when H_2 receptors are blocked, unopposed activation of H_1 receptors by histamine may cause bronchospasm.
- Cimetidine inhibits hepatic microsomal enzymes; therefore, theophylline metabolism is decreased and its toxicity is increased.

Intraoperative Management

Monitoring: Standard monitors.

Pulsus paradoxus is a systemic blood pressure deficit measured during the spontaneous ventilatory cycle. A paradox of greater than 10 mm Hg (1.3 KPa) **indicates severe asthma**.

Choice of Anesthesia:

A. Regional Anesthesia: Controversy exists.

Advantage: - It avoids instrumentation of the airway.
- It allows good postoperative analgesia and more effective cough.

Disadvantages:

1. High spinal or epidural anesthesia (above T6) can:

• increase bronchospasm by blocking the sympathetic tone; therefore, unopposed parasympathetic activity occurs.

• decrease expiratory reserve volume (by 48%) and decrease use of accessory respiratory muscles. This produces ineffective cough and retention of secretions which increases postoperative respiratory complications.

2. It can not control ventilation as general anesthesia does.

B. General Anesthesia:

Aim:

1- It avoids pain, emotional stress, and light anesthesia which precipitate bronchospasm.

2- The most critical time for an asthmatic patient is instrumentation of the airway.

3- Avoided drugs include those causing: ▫ Bronchospasm e.g., β_2 blockers.
▫ Histamine release e.g., curare, atracurium, and morphine.

Induction:

Smooth induction (and emergence)

- Good pre-oxygenation.

- Induction agents:

The most important thing is to achieve depth of anesthesia than to choose the agent.

• Methohexital, propofol or etomidate are preferred as they cause no histamine release.

• Thiopentone is the most commonly used in adults, but occasionally induces bronchospasm due to exaggerated histamine release.

• Ketamine: i.v. (of choice).

- It causes a bronchodilator effect (dose-independent) due to inhibition of noradrenaline reuptake which stimulates the sympathetic system.
- It should **not** be used in patients **with** high **theophylline** levels as the combined actions of both drugs precipitate **seizure** activity.

• Halothane, enflurane or sevoflurane are drugs of choice as induction agents in children because they have bronchodilator effects.

• Isoflurane or desflurane produce the same bronchodilator effect, but they must be increased slowly with care because they exert a mild irritant effect on the airways.

- **Succinylcholine:** Although it produces marked histamine release, it is used safely in asthmatic patients.

To Blunt Reflex Bronchospasm Induced by Intubation:

1- Additional dose of thiopentone 1-2 mg/kg.
2- Ventilating with 2-3 MAC volatile agent for 5 min.
3- Lidocaine - I.v. 1-2 mg/kg 1-2 min before intubation.
- Intra-tracheal 1-2 mg/kg just before intubation, but it can induce bronchospasm if an inadequate induction dose of thiopentone is used.
- Spray over the larynx and trachea just before intubation.
4- A β_2 adrenergic agonist inhaler prior to the induction of anesthesia.

- To assess intubation: - capnography.
- auscultation (may be difficult if there is marked bronchospasm).

- Laryngeal mask airway is a very suitable choice because it decreases bronchospasm when compared to endotracheal intubation.

Maintenance:

Volatile anesthetics ± N_2O + muscle relaxant + controlled ventilation

Volatile anesthetics:

They are the most suitable due to their potent bronchodilating effect (sevoflurane has the same bronchodilator effect as halothane).

It is more important to achieve depth of anesthesia rather than to choose the agent.

In elderly COPD, asthmatic patients or cardiac patients who can not tolerate the depth of anesthesia, lidocaine infusion 1-2 mg/kg/hour is used.

Avoid halothane as:
- It sensitizes the heart to aminophylline and β_2 agonists (other agents do not sensitize the heart).
- It increases the incidence of arrhythmias in presence of hypercapnia as in status asthmaticus or COPD.

N_2O: is used with care. It should be avoided in patients with:
- Large bullae which may rupture and cause tension pneumothorax.
- Pulmonary hypertension which may be increased and cause pulmonary edema.

Muscle relaxants:

Pancuronium, vecuronium, cis-atracurium, and rocuronium are drugs of choice.

Avoid d-tubocurarine and others which cause histamine release.

Although atracurium causes histamine release, it can be used safely in most asthmatic patients especially if given slowly.

Controlled ventilation:

It is performed with warmed, humidified gases whenever possible to prevent inspissation of dried secretions.

Adjust ventilation parameters as follows:
- Tidal volume: 10-15 mL/kg, slightly more than normal to allow optimal ventilation/perfusion matching.
- Respiratory rate: 6-10 breaths/min, slightly less than normal to allow sufficient time for venous return to the heart.
- Relatively short inspiratory time and relatively long expiratory time i.e., I: E ratio to be > 1: 2 (up to 1: 3) with increasing inspiratory gas flow rate to avoid air trapping in the lung.
- Low inflating pressure: to avoid barotrauma especially in presence of bullae.

Positive end expiratory pressure (PEEP) should be avoided.

Air Trapping (Auto-PEEP or Intrinsic PEEP):

• It occurs in severe asthmatic patients or those with COPD who have increased airway resistance (**severe bronchospasm**) and **ventilated mechanically** with **short expiratory time**; therefore, there is insufficient

time for expiration, causing air trapping which causes more increase in airway pressure. This decreases venous return especially in marginal volume status patients producing hypotension.

• If the **pulse pressure falls** and **neck veins** appear **distended**, consider obstructed venous return and a dependent **fall in cardiac output**. **Disconnect the endotracheal tube** intermittently from the circuit and observe the connected capnogram trace for evidence of prolonged expiration and return of pulse pressure to its previous level.

Intraoperative Fluid:

It should be **generous** to maintain adequate hydration. It causes less viscid secretions to be easily expelled from the airway.

Intraoperative Complications:

Intraoperative Bronchospasm

Causes:

• Light anesthesia, straining, or traction on viscera causing vagal stimulation.

• Endotracheal tube: ▫ Touching carina.
▫ Endobronchial intubation.
▫ Tube obstruction e.g., over-inflation of the balloon, kinking, and secretions.

• Lung: ▫ Aspiration. ▫ Pneumothorax.
▫ Pulmonary edema. ▫ Pulmonary embolism.

• Drugs: - Ether ▫ Trichloroethylene (irritant).

• A patient in acute asthmatic attack.

Manifested by:

• Wheezes.

• Slowly rising wave on capnography, the severity of obstruction is generally inversely related to the rate of rise in the end-tidal CO_2 (figure 12-25).

• Increased peak inspiratory pressure.

• Incomplete expiration (i.e., decreased expiratory tidal volume).

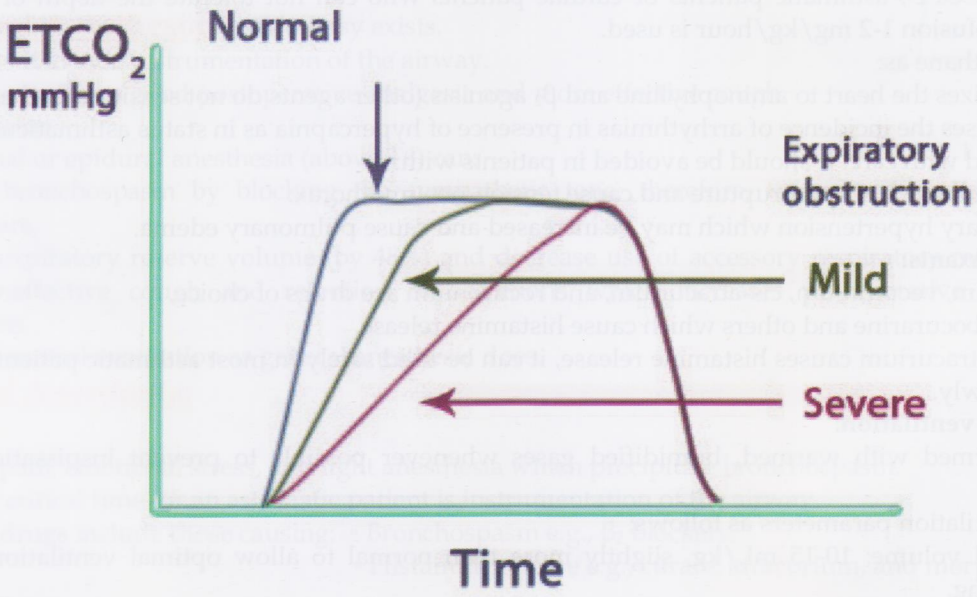


Figure 12-25: Capnograph of airway obstruction

Management:

1- Assess the cause of bronchospasm at first.

2- Increase the depth of anesthesia by volatile agents (after measuring blood pressure).

3- Mild bronchospasm is treated by a β_2 agonist aerosol put into the inspiratory limb of the breathing circuit.

4- Moderate to severe bronchospasm is treated by:

• Aminophylline i.v. slowly, with electrocardiogram (ECG) monitoring. It causes dysrhythmia especially with halothane.
- If the patient was not receiving preoperative aminophylline, give a 6 mg/kg bolus over 20 min followed by 0.5-0.9 mg/kg/hour.
- If the patient was receiving preoperative aminophylline give ¼ - ½ the previous doses according to aminophylline plasma level.
N.B.: General anesthesia decreases hepatic blood flow by 30%; so, it is advisable to decrease the rate of infusion of aminophylline by 30% to compensate for the decrease in its metabolism.

• β_2 agonist as - Terbutaline subcutaneous 0.25 mg or metered inhaler aerosol.
- Salbutamol nebulizer by positive pressure ventilation
or slowly i.v. 125-250 µg with ECG monitoring.
• Hydrocortisone i.v. 100-200 mg.
• Ketamine i.v.
• I.v. or subcutaneous epinephrine or isopreternol if other measures fail.
5- Finally, if there is still severe spasm, use **an intensive care ventilator** which can provide high inspiratory pressure (in front of high airway resistance) e.g., 120 cm H_2O, but inhalational agents can not be used, therefore, **total intravenous anesthesia (TIVA)** can be used instead. Recently, there are anesthetic machines with an intensive care ventilator and also intensive care ventilators with a vaporizer and O_2 mixer.

Recovery:

Reversal of non-depolarizing muscle relaxants with anti-cholinesterase agents can induce bronchospasm, but this does not occur if it is preceded by the appropriate dose of an anti-cholinergic agent.
Deep extubation, before returning of airway reflexes, decreases the risk of bronchospasm.
If awake extubation is indicated, lidocaine 1-2 mg/kg i.v or 1-2 mg/kg/hour i.v. infusion is given to blunt airway reflexes.

Postoperative Management and Intensive Care Considerations:

Close respiratory monitoring is needed. Patients with severe disease should be managed in intensive care units as follows:
1. Humidified oxygenation: In asthmatic patients, there is no hypoxic drive or CO_2 retention; so, high inspired O_2 can be tolerated and monitored by pulse oximetry.
2. Position: Semi-sitting or sitting upright in a chair is indicated as soon as possible.
3. Elective postoperative controlled ventilation is rarely needed
Indications: severe and very severe bronchial asthma (as above).
- $PaCO_2 > 50$ mm Hg.
- $PaO_2 < 50$ mm Hg + dyspnea at rest.
- Pulmonary function tests are < 50 % of predicted.

4. Adequate analgesia: is achieved by:
• Simple non-opioid analgesics as non-steroidal anti-inflammatory drugs (NSAIDs). Care should be taken with NSAIDs because they can cause bronchial asthma.
• Opioid analgesics: - Better to be avoided and if used, they should be under supervision.
- Pethidine is preferred to morphine.
- Patient controlled analgesia.
• Local or regional techniques.
• Transcutaneous Electrical Nerve Stimulation (TENS)
Value: Pain may compromise respiration especially after abdominal or thoracic surgery.
5. Continue treatment postoperatively as bronchodilators, antibiotics, and physiotherapy.

Chronic Obstructive Pulmonary Disease (COPD)

Pathogenesis:

It is classified into a chronic bronchitic group and an emphysematous group representing the two extremes, but most patients are in between with mixed features.

	Chronic Bronchitis (Blue Bloater Syndrome)	Emphysema (Pink Puffer Syndrome)
Cause	- Smoking (the commonest) - Air pollutants - Recurrent chest infection	- Smoking (the commonest) - Homozygous α_1 anti-trypsin deficiency: α_1 anti-trypsin is a protease inhibitor that prevents the proteolytic activity of enzymes (mainly elastase) in lungs; these enzymes are produced by pulmonary neutrophils and macrophages in response to infection and pollutants.
Pathology	- **Chronic irritation** causes: • **Bronchospasm** (the term chronic asthmatic bronchitis is used when bronchospasm is a major feature). • Hypertrophy of bronchial mucous glands with **increased secretions.** • **Inflammation with bronchial edema** causing airway obstruction (increased airway resistance). At first, it is reversible then becomes irreversible (elastic recoil is normal). - When CO_2 retention occurs, the normal ventilatory drive becomes mainly dependent on the hypoxic drive. - Hypoxia causes early corpulmonale.	- There is: • **Destruction of alveolar septa** which causes irreversible enlargement of the airways distal to the terminal bronchioles. • **Loss of elastic recoil** (that normally supports small airways by radial traction). This causes premature collapse during expiration. • **Destruction of pulmonary capillaries in alveolar septa** which decreases the diffusion capacity and causes pulmonary hypertension. Corpulmonale occurs later (normal airway resistance).
Clinical Picture **- Cough** **- Dyspnea** **- Sputum** **- Corpulmonale**	 - Productive cough on most days of 3 consecutive months for at least 2 consecutive years - Little and mild - Copious - Early	 - With exertion - Marked, patients often purse their lips to delay closure of small airways, hence the name - Scant - Late
Investigation - Hct - $PaCO_2$ (mmHg) - PaO_2 (mmHg) - Chest x-ray	Due to hypoxia and hypercapnia - ↑ - ↑ > 40 - ↓ < 60 - ↑ lung vascular markings due to inflammation	Due to dyspnea - Normal - Normal or ↓ < 40 - Normal or ↑ > 60 - Picture of emphysema as hyperinflation...etc.
Prognosis	Poor	Good

Preoperative Management:

The same assessment is performed as bronchial asthma.

The Global initiative for chronic Obstructive Lung Diseases (GOLD) guidelines

It is used for diagnosis and classification of the severity of patients with COPD and is based on post-bronchodilator FEV_1

Stage	Characteristics
0:	• Normal spirometry • Chronic symptoms (cough, sputum production)
I: Mild COPD	• $FEV_1/FVC < 70\%$ • $FEV_1 \geq 80\%$ of predicted • With or without chronic symptoms (cough, sputum).
II: Moderate COPD	• $FEV_1/FVC < 70\%$ • FEV_1 50-79% of predicted • With or without chronic symptoms (cough, sputum).
III: Severe COPD	• $FEV_1/FVC < 70\%$ • FEV_1 30-49% of predicted • With or without chronic symptoms (cough, sputum).
IV: Very severe COPD	• $FEV_1/FVC < 70\%$ + • $FEV_1 < 30\%$ of predicted or • $FEV_1 < 50\%$ of predicted with chronic hypoxemia and hypercapnia.

BODE Index

It is used for preoperative prediction of postoperative outcome

	0	1	2	3
B: body mass index	< 21	≥ 21		
O: obstruction FEV_1 (% of predicted)	≥ 65	50-64	36-49	≤ 35
D: dyspnea scale	0-1	2	3	4
E: exercise capacity as assessed by the 6-minute walk test (meters)	≥ 350	250-349	150-249	≤ 149

The more the points are, the worse the prognosis is.

Intraoperative Management:

A. Regional Anesthesia:

- Advantages and disadvantages are as the bronchial asthma (see above).
- The axillary route of the brachial plexus blockade is preferred because:
  - the supra-clavicular route is associated with more possibility of pneumothorax as the chest is emphysematous.
  - the interscalene route is associated with more possibility of phrenic nerve blockade.

B. General Anesthesia

- The same precautions are taken as bronchial asthma.
- Hypercapnia secondary to chronic hypoventilation should not be corrected intraoperatively because it may be difficult to wean the patient from mechanical ventilation as a result of the decreased respiratory drive in patients who are chronically hypoventilated.

Postoperative Management and Intensive Care Considerations:

Close respiratory monitoring is essential. Patients with severe disease should be managed in intensive care.

1. Humidified oxygenation:

If the patient has **CO_2 retention and a hypoxic drive**, the patient can not tolerate high inspired O_2. Therefore, the aim is to maintain:

- SaO_2 > 90% and PaO_2 = 60-80 mm Hg.
- $PaCO_2$ < 55-60 mm Hg and pH 7.35-7.45.

Frequent monitoring with pulse oximetry and arterial blood gases is essential.
Therefore, FiO_2 is titrated either by:

- Venturi mask, usually at 24-28 % (1-2 L/min).
- Mechanical ventilation.

2. Position:

Semi-sitting or sitting upright in a chair is indicated as soon as possible.

3. Elective postoperative controlled ventilation:

- Indications: Patients with severe or very severe COPD who are at a greatest risk postoperatively:
  - Preoperative $PaCO_2$ > 50 mm Hg.
  - Preoperative PaO_2 < 50 mm Hg.
  - Preoperative pulmonary function tests are < 50 % predicted.
- This possibility should be discussed with the patient and the surgeon preoperatively.
- PEEP is used only if PaO_2 can not be increased > 60 mm Hg with 50% O_2, but it causes air trapping.
- Advantages: It allows:

1- Adequate oxygenation.
2- Adequate analgesia without fear of opioid-induced respiratory depression.
3- Clearance of secretions by physiotherapy, and tracheal suction by fiberoptic bronchoscopy.
4- Correction of cardiac output, peripheral perfusion and fluid overload before restoration of spontaneous ventilation.

- Unless there is preexisting pulmonary infection, a period of 24 hours of elective controlled ventilation is usually adequate.

4. Adequate analgesia.

5. Continue treatment postoperatively:

The same as bronchial asthma.

6. Breathing exercise (inspiratory exercise):

- It is either:
  - Voluntary deep breathing.
  - Incentive spirometry: It is a type of voluntary deep breathing in which the patient is given inspired volumes as a goal to achieve.

Both cause re-expansion of collapsed alveoli.

N.B.: Expiratory maneuvers: as inflating balloons, the use of blow bottles or performing FVC are not recommended because they make patients exhale below the FRC which generates pleural pressure that exceeds airway pressure and causes collapse of alveoli.

7. Continuous Positive Airway Pressure (CPAP):

It is performed by either nasal or face mask. In a spontaneously breathing patient, CPAP increases the FRC and decreases atelectasis; therefore, it decreases the need for mechanical ventilation.

8. Mini-tracheostomy: Percutaneous cricothyroid puncture and insertion of a small diameter tube into the trachea are done. This allows aspiration of secretions and preserves the ability to cough and speak. It is very rarely needed.

Other Obstructive Pulmonary Diseases

	Bronchiectasis	Cystic fibrosis	Kartagner Syndrome	Bronchiolitis Obliterans	Tracheal Stenosis
Pathology	It is a localized and irreversible dilatation of a bronchus caused by **destructive inflammatory processes** involving the bronchial walls e.g., untreated or inadequately treated broncho-pneumonia.	It is inherited as an **autosomal recessive** disease. There is a **defect in chloride transport** which increases viscosity of all exocrine glands. This causes obstruction of these glands.	It is inherited as an **autosomal recessive** disease. There is primary ciliary dyskinesia.	It causes chronic airflow obstruction in adults due to: • Viral pneumonia • Collagen vascular diseases especially rheumatoid arthritis • Nitrogen dioxide inhalation "silo-fillers disease". • As a consequence of graft-versus-host disease of bone marrow transplantation.	Prolonged trans-laryngeal (oral or nasal tracheal) intubation or tracheostomy causes tracheal mucosal ischemia which produces destruction of cartilaginous rings. A circumferential constricting scar is produced. If the trachea of an adult is < 5 mm in diameter, symptoms appear.
Clinical picture	- Productive cough with purulent sputum. - Recurrent hemoptysis. - Recurrent bacterial infection. - Hypoxia causing clubbing of fingers. **- Chest x-ray shows honey comb appearance** (figure 12-26). - Pulmonary function tests: unpredictable ranging between **COPD and restrictive lung disease.**	- Obstruction of **tracheo-bronchial tree** by secretions which plug the bronchi causing expiratory obstruction and 2ry infection. Therefore, chronic productive cough, purulent sputum, and recurrent hemoptysis occur. - Obstruction of **pancreatic ducts** causes pancreatic insufficiency. - Obstruction of **bile duct** causes hepatic cirrhosis, and portal hypertension and decreases absorption of fat soluble vitamins. So, vitamin K deficiency occurs resulting in risk of hemorrhage.	**- Bronchiectasis** ... etc. **- Chronic sinusitis** producing chronic otitis media. **- Situs inversus** (dextrocardia).	- Dyspnea - Nonproductive cough. - Non-cardiogenic pulmonary edema.	- Symptoms occur usually after extubation after several weeks of intubation causing COPD (see flow volume loops).

Anesthetic management	1. It is treated by antibiotics and postural drainage 2. Surgical resection if it is localized by using double lumen endo-bronchial tube. This is done to prevent spillage of purulent sputum into normal areas of the lung.	The same as COPD + 1. Vitamin K replacement 2. Aggressive suctioning intra-operatively, before extubation, and postoperatively. 3. Amiloride aerosol: It blocks the associated increased Na^+ reabsorption.	1. Bronchiectasis 2. Chronic sinusitis: - Avoid naso-pharyngeal airway. 3. Dextrocardia: - Reverse ECG leads to permit accurate interpretation. - During labor, right uterine displacement is done (instead of left).	1. Corticosteroids 2. Bronchodilators.	Surgical resection (nearly the same as laryngeal resection) (see later).

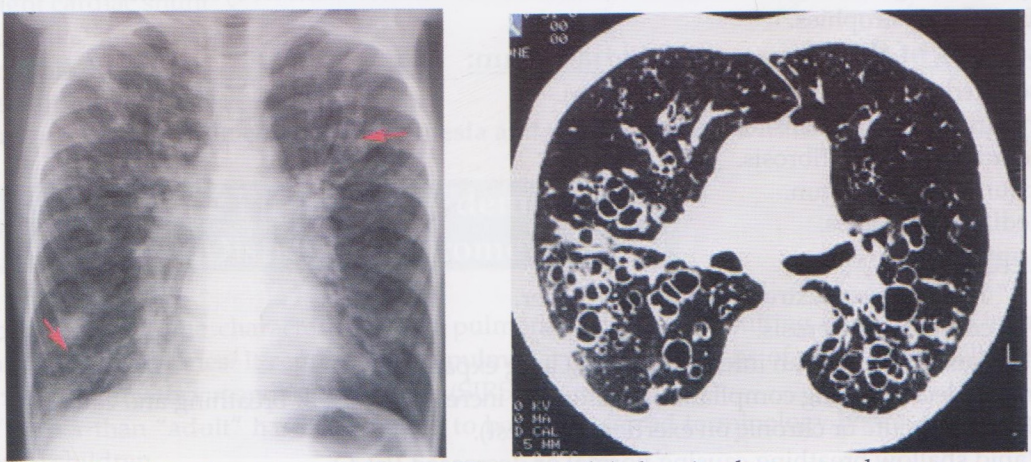


Figure 12-26: Plain chest x-ray (left) and CT scan (right) showing honey comb appearance of bronchiectasis

Restrictive Pulmonary Diseases

Causes:

A. Acute Intrinsic Restrictive Lung Diseases (Pulmonary Edema):

(It is associated with increased extracellular lung water).

a. Cardiogenic pulmonary edema: congestive heart failure (high pressure pulmonary edema).

b. Non-cardiogenic (exudative) pulmonary edema (low pressure pulmonary edema):

1. Adult respiratory distress syndrome.
2. Aspiration pneumonitis.
3. Neurogenic pulmonary edema.
4. High altitude pulmonary edema.
5. Negative pressure pulmonary edema.
6. Drug-induced pulmonary edema.
7. Re-expansion of collapsed lung.
8. Lateral decubitus (unilateral) pulmonary edema due to effect of gravity which pools fluids into the dependent lung.

B. Chronic Intrinsic Restrictive Lung Diseases (Interstitial Lung Disease):

(It is associated with increased lung fibrosis).

- Sarcoidosis.
- Pulmonary alveolar proteinosis.
- Diffuse idiopathic pulmonary fibrosis.
- Drug induced pulmonary fibrosis as bleomycin, methotrexate, and busulphan.
- Esinophilic granuloma (Histocytosis X).

- Radiation pneumonitis.

C. Chronic Extrinsic Restrictive Lung Diseases:

(It is associated with decreased lung expansion).

a) Disorders of the chest wall:

- Obesity.
- Flail chest e.g., parallel vertical multiple ribs fracture or separation of a median sternotomy after cardiac surgery.
- Deformity of the sternum as pectus excavatum.
- Kyphoscoliosis.
- Ankylosing spondylitis.

b) Increased intra-abdominal pressure:

- Ascites.
- Pregnancy.

c) Neuromuscular disorders:

- Spinal cord transection.
- Myasthenia gravis.
- Muscular dystrophies.
- Guillian Barré syndrome.
- Eaton-Lambert syndrome.

D. Disorders of the Pleura and Mediastinum:

(It is associated with decreased lung expansion).

- Pneumothorax and tension pneumothorax.
- Pleural effusion or fibrosis.
- Pneumo-mediastinum.
- Mediastinal masses.

Pathology:

Group "A" has increased extra-vascular lung water.
Group "B" causes lung fibrosis.
Groups "C" and "D" cause an interference with lung expansion.
Therefore, all decrease lung compliance, resulting in increased work of breathing and cause:

- Dyspnea (acute or chronic on exertion or at rest).
- Rapid shallow breathing causing normal or decreased $PaCO_2$.
- Hypoxia.

Destruction of pulmonary vasculature in chronic restrictive lung diseases causes pulmonary hypertension and corpulmonale.

Anesthetic Management:

Preoperative Management:

Preoperative Evaluation:

- Clinical picture of restrictive lung diseases should be evaluated such as dyspnea and rapid shallow breathing.
- The cause of restrictive lung disease should be assessed and managed.
- Preoperative investigations: are discussed above.

Preoperative Patient Preparation: is discussed above.

Intra-operative Management:

A. Regional Anesthesia:

Avoid a high sensory level above T_{10} to maintain acceptable ventilation.

B. General Anesthesia:

- Maintenance: i.v and inhalational agents can be used safely.
- Mechanical ventilation is used with the following precautions:
  - Tidal volume: 8-10 mL/kg (slightly less than normal).
  - Respiratory rate: 14-18 breaths/min (slightly more than normal).
  - Peak airway pressure: should not be increased > 40 cm H_2O due to decreased lung compliance as it may increase the risk of barotrauma.
  - PEEP: may be required.
  - Other modes of ventilation may be needed in severe cases: see later.

Postoperative Management:

Elective controlled ventilation may be needed.

Pulmonary Edema

Definition:

It is transudation of fluid first from pulmonary capillaries into the interstitial space and then from the interstitial space into the alveoli due to either:

- Increased pulmonary capillary pressure (high pressure pulmonary edema)
  i.e., cardiogenic pulmonary edema.

or - Increased pulmonary capillary permeability (low pressure pulmonary edema)
  i.e., non-cardiogenic pulmonary edema.

I. Cardiogenic (Hemodynamic) Pulmonary Edema

Causes:

1- Pulmonary venous hypertension (congestion) due to mitral stenosis, left ventricular failure, and left atrial obstruction.

2- Marked increase in pulmonary blood flow due to:

- Left to right cardiac shunt
- Severe anemia.
- Hypervolemia.
- Severe exercise.

More details are discussed in chapter "Anesthesia and Cardiovascular Diseases".

II. Non-Cardiogenic Pulmonary Edema
Acute Respiratory Distress Syndrome (ARDS)

Definition:

- It is a clinical syndrome characterized by a pulmonary disorder resulting from diffuse injury to the alveolo-capillary membranes. It represents the pulmonary manifestations of a pan-endothelial insult due to a systemic inflammatory response syndrome (SIRS).
- "Acute" rather than "adult" has been agreed to be the preferred terminology because the same picture is also seen in children.

It has been previously called - Post-traumatic pulmonary insufficiency syndrome,
- Shock lung syndrome,
- Wet lung syndrome, or
- Stiff lung syndrome.

Criteria of ARDS:

There is an acute onset of the following criteria:

1- Decreased gas exchange (PaO_2/ FiO_2 < 200 mm Hg) i.e., refractory hypoxemia.

2- Diffuse bilateral (3 or 4 quadrant) airspace infiltrates on chest radiograph (< 7 days old).

3- Exclusion of high pressure pulmonary edema (cardiogenic pulmonary edema) where pulmonary capillary wedge pressure is less than 18 mm Hg and there is no clinical evidence of left ventricular failure.

In addition to the old criteria:

1- Bedside findings of tachypnea, dyspnea and crackles.

2- Decreased compliance < 40 mL/cm H_2O.

On the basis of appropriate clinical judgment, an individual patient may be diagnosed as having ARDS and treated accordingly without meeting all criteria.

Difference between ARDS and Acute Lung Injury (ALI)

Both have the **same clinical picture**, but with the following differences:

ARDS	ALI
More severe form	Less severe form
Severe hypoxemia PaO_2/ FiO_2 < 200 mm Hg	PaO_2/ FiO_2 = 200-300 mm Hg

ARDS is a combination of severe ALI, non-cardiogenic pulmonary edema, and fibro-proliferation with collagen deposition.

Clinically, the distinction between ARDS and ALI is not important.

Causes:

	Pulmonary (Direct, Primary) ARDS	Extra-Pulmonary (Indirect, Secondary) ARDS
Causes	1. Thoracic trauma: - Lung contusion or chest trauma. - Blast injury. - Post-pneumonectomy. 2. Aspiration pneumonitis. 3. Near drowning. 4. Severe pneumonia (bacterial, viral, protozoal). 5. Thoracic irradiation. 6. Smoke or toxic gas inhalation. 7. O_2 toxicity.	1. Non-thoracic trauma: - Multiple severe trauma - Head injury - Massive burn 2. Circulatory shock. 3. Septicemia (especially gram negative). 4. Multi-organ dysfunction syndrome (MODS). 5. Massive blood transfusion or even after single blood transfusion where transfusion-related acute lung injury (TRALi) may occur. 6. Fat embolism. 7. Amniotic fluid embolism. 8. Pancreatitis (release of proteinase and lipase causing damage of the pulmonary capillary endothelium). 9. Disseminated intravascular coagulation (DIC). 10. Malaria. 11. Drug overdosage or poisoning such as opioids (heroin), salicylates, amiodarone, busulphan, or bleomycin. 12. Post-cardiopulmonary bypass. 13. Tumor lysis syndrome. **These are the causes of SIRS.**

Pathogenesis:

• ARDS represents the pulmonary manifestations of a systemic inflammatory response syndrome (SIRS) which includes release of large amounts of **cytokines** and other 2ry mediators like tumor necrosing factor, interleukin 1, 2, 6, and 8, platelet activation factors and various prostaglandins, **nitric oxide (NO), endothelin** and leukotrienes. These increase capillary permeability all over the body (figure 12-27).

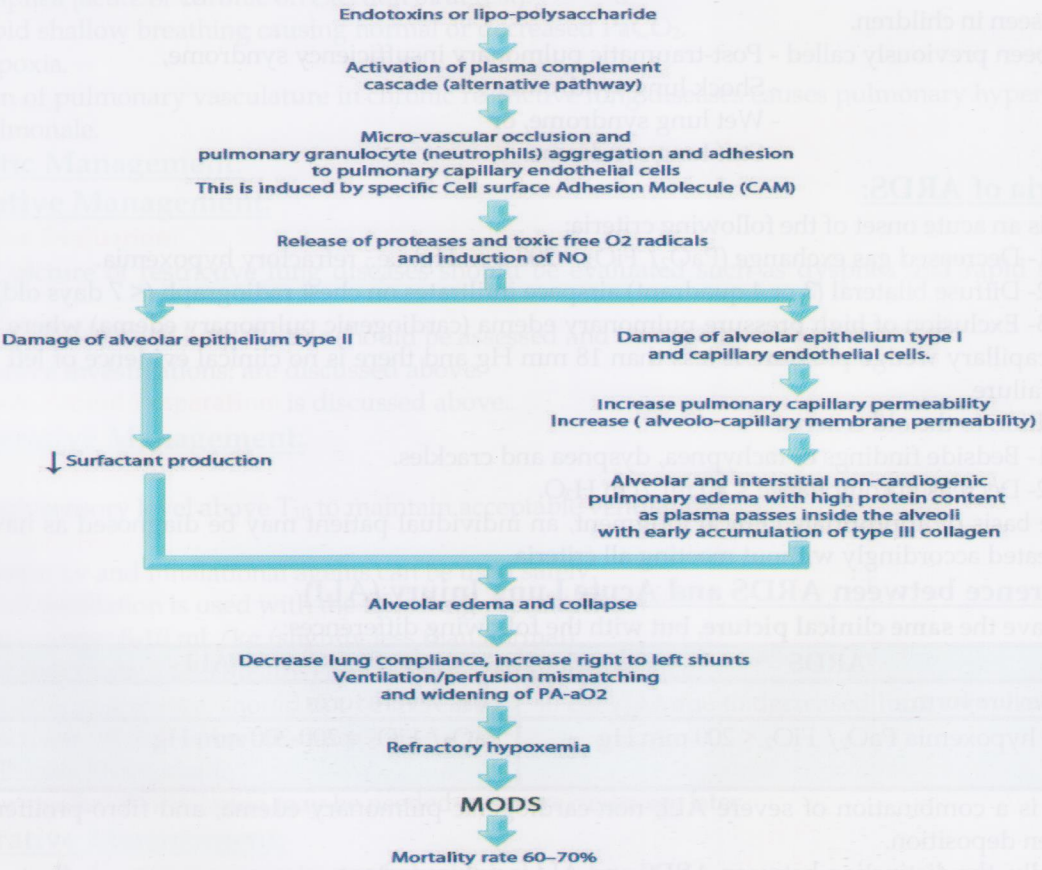


Figure 12-27: Pathogenesis of ARDS

• There are differences in the pathology of pulmonary and extra-pulmonary ARDS:

	Pulmonary ARDS	Extra-pulmonary ARDS
Pathology	The main pathology is: • **Consolidation**, with alveolar filling with fibrin, edema, blood cells, and collagen. • **Stiffness of the lungs** Therefore, ventilation does **not improve with application of PEEP.**	The main pathology is: • **Atelectasis** of alveolar architecture accompanied by micro-vascular congestion • **Stiffness of thoraco-abdominal cage** (with less lung stiffness). Therefore, ventilation improves with application of PEEP.

• **Theories of Development of Multiple Organ Dysfunction Syndrome (MODS):**

1- The same systemic process that damages the lungs injures other organs.
2- Refractory hypoxemia.
3- The therapy of ARDS by positive pressure ventilation and PEEP although they improve lungs, they decrease cardiac output and oxygen delivery (the most accepted theory).

Course of ARDS:

The onset is acute, but there is usually **a latent period** of hours or days during which the damage is minimal or slowly progressive.
ARDS passes in 2 phases:
An exudative phase (1-7 days): in which alveolar edema and collapse occur, causing severe progressive respiratory failure which needs mechanical ventilation.
A fibrotic or proliferative phase (7-21 days): It is also called **chronic lung injury.**
It follows the exudative phase in surviving patients, in which fibrosing alveolitis occurs with hyaline membrane formation followed by **irreversible pulmonary fibrosis**. This occurs due to **deposition of type III collagen** in alveolar and interstitial spaces. Later on, **restrictive lung disease** occurs.

Clinical Picture:

• Clinical picture of the cause such as fever, hypotension, trauma…etc. In 5- 10% the cause may be unrecognized.
• Progressive dyspnea, tachypnea, rales, wheezes, cyanosis up to respiratory failure.
• Progressive tachycardia, cardiac dysrhythmia, and hypotension.
• Multi-organ dysfunction syndrome (MODS): It occurs in critically ill or injured patients. There is a hyperdynamic and hyper-metabolic state (similar to sepsis). The sequence of organ failure in most patients is as follows: the lung (the 1st organ to fail), the liver, the kidney, gastrointestinal mucosa (it loses its barrier against luminal bacteria), the heart (ventricular wall motion abnormalities despite increased cardiac output), and lastly central nervous system dysfunction occurs. Death is the fate in 100% of cases if more than 3 organs fail.

Investigations:

1. Arterial blood gases show:
• Severe refractory hypoxemia even after 100% O_2 as PaO_2 is not raised above 60-100 mm Hg.
• pH is high, normal, or low depending on the ability of the patient to maintaining $PaCO_2$.
2. Chest x-ray shows: bilateral interstitial fluffy pulmonary infiltrates, which may progress to complete opacification. It is an essential monitor in intensive care (figure 12-28).

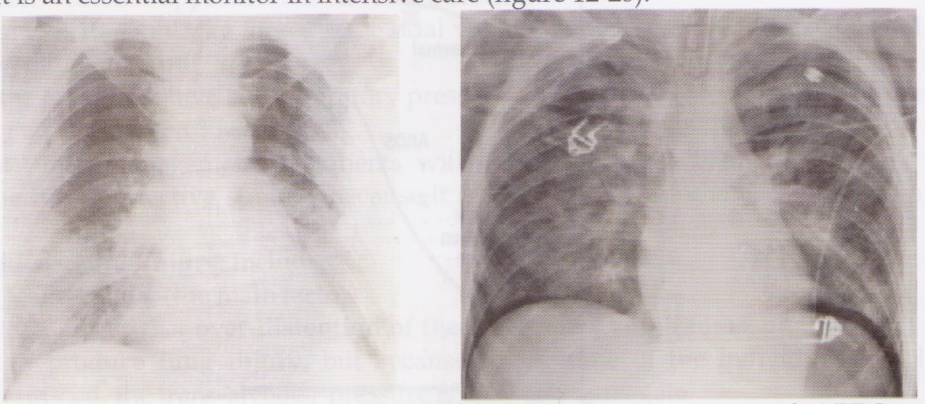


Figure 12-28: Two different plain chest x-rays of two patients with ARDS

3. CT scan shows:

Pulmonary ARDS	Extra-Pulmonary ARDS
• **Ground-glass opacification.** • **Consolidation** (it is due to direct lung injury. It is the area responsible for the decreased PaO_2, increased shunt fraction, increased mean pulmonary arterial pressure). **Both are equally prevalent.**	• **Ground-glass opacification predominantly** (it represents a combination of edema, atelectasis or early hyaline membrane formation). It is due to the systemic effects of lung injury (figure 12-29).

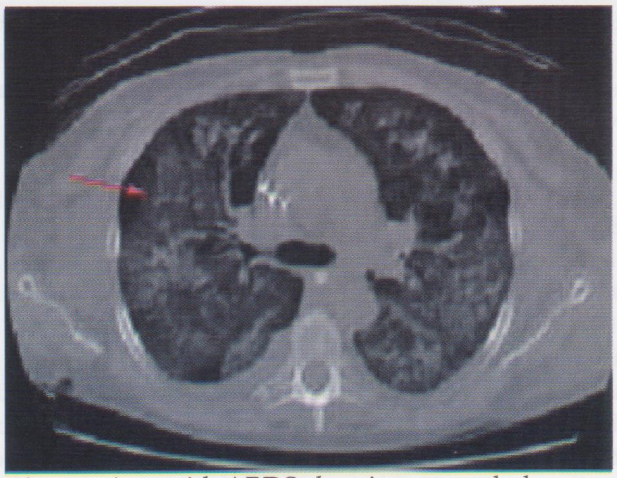


Figure 12-29: CT scan in a patient with ARDS showing ground glass appearance (arrow) and alveolar infiltrations

4. Pulmonary artery catheter.

• Pulmonary capillary wedge pressure (PCWP) is normal or decreased unless there is congestive heart failure.

• Pulmonary artery pressure (PAP) may show pulmonary hypertension due to obliteration of capillaries by fibrotic changes.

5. Pulmonary function tests: **compliance curve**

Routine use of compliance curves is not practical for technical and clinical uses during management of ARDS. The curve is shifted downward and rightward where the compliance decreases and greater pressure is needed to inflate the lungs and the work of breathing is increased. Application of PEEP improves lung compliance and the curve returns to its normal position especially in extra-pulmonary ARDS where atelectasis is the main pathology (figure 12-30).

6. Other investigations of the cause or MODS e.g. renal, hepatic, and electrolyte disturbances.

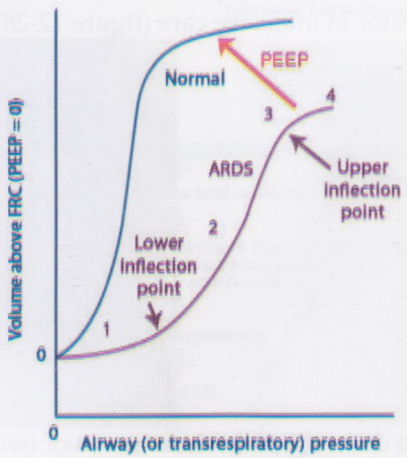


Figure 12-30: Effect of PEEP on the compliance curve of ARDS

Differential Diagnosis:

Clinical differential diagnosis between cardiogenic and non-cardiogenic pulmonary edema

	Non-Cardiogenic Pulmonary Edema	Cardiogenic Pulmonary Edema
Clinical picture	• Pulmonary or non-pulmonary infection, or history of aspiration • Hyperdynamic state. • High white-cell count. • Evidence of pancreatitis or peritonitis. • Brain natriuretic peptide level < 100 pg/mL. • Negative fluid balance.	• History of myocardial infarction or congestive heart failure. • Low cardiac output state, third heart sound, peripheral edema, jugular venous distention. • Elevated cardiac enzymes. • Brain natriuretic peptide level > 399 pg/mL. • Positive fluid balance.
Chest radiograph	• Normal cardiac size. • Vascular pedicle width < 70 mm and no central peri-hilar prominence. •Peripheral distribution of infiltrates. • Absence of Kerley's B lines. • Absence of pleural effusion, but still may occur.	• Enlarged cardiac size i.e., cardiomegaly. • Vascular pedicle width > 70 mm and central peri-hilar prominence is present. • Central distribution of infiltrates. • Presence of Kerley's B lines. • Prominent pleural effusion.
Trans-thoracic or trans-esophageal echo-cardiogram	• Normal or small cardiac chamber sizes. • Normal left ventricular function.	• Enlarged cardiac chambers. • Decreased left ventricular function.
Pulmonary artery catheterization	• PCWP < 18 mm Hg	• PCWP > 18 mm Hg
Broncho-alveolar lavage	The lavage fluid is very rich in: • Neutrophils > 80% of cells. • Proteins as it is lung inflammation (> 70% of that protein concentration in serum i.e., protein lavage/serum ratio is > 0.7).	The lavage fluid contains: • Neutrophils < 5% • Proteins (< 50% of protein in serum i.e., protein lavage/serum ratio is < 0.5).

N.B.: Broncho-alveolar lavage is done by a flexible fiberoptic bronchoscope and saline irrigation. It is the most reliable method for confirming the diagnosis, but is rarely used. In pneumonia, both neutrophils and protein concentration are as that of ARDS; so, pneumonia should be excluded at first.

Management and Intensive Care Considerations: in intensive care units.

I. O_2 Therapy:

- Initially PaO_2 can be maintained while $PaCO_2$ is decreased, but when ARDS worsens, even 100 % O_2 may not prevent hypoxemia and hypercapnia.
- O_2 can be administered by a nasal cannula, Venturi mask, non-rebreathing mask, or T-piece, but most patients require mechanical ventilation.
- The FiO_2 should be lowered as soon as possible to less than 0.5 to reduce the risk of lung damage from O_2 toxicity.

II. Ventilation Management:

In the past, a conventional approach was used. It included:

- A tidal volume of 10-15 mL/kg. It is a large tidal volume, which is twice the size of tidal volume used during quiet breathing (6-7 mL/kg).
- Selection of the lowest positive end expiratory pressure (PEEP) to achieve adequate oxygenation.
- Keeping the $PaCO_2$ between 35-38 mm Hg.

Recently, ventilatory management of patients with ARDS has been changed from the conventional approach to the **lung protective strategy** because it is apparent that mechanical ventilation induces lung injury.

Ventilator Induced Lung Injury: includes:

1- Pulmonary Volutrauma: (the main factor)

- Many researches prove that **over-distention of the alveoli i.e., volutrauma,** and not high pressures i.e., barotrauma, **can produce lung injury**, but because the volume of the individual alveolus cannot be practically determined, the trans-alveolar pressure is used as a surrogate.

• Excessive inflation **volumes above upper inflection point** produce stress fractures in the alveolar capillary interface and rupture of the distal airspaces. This leads to infiltration of the distal airspaces with inflammatory cells and proteinaceous material.

2- Shear Stress:

• In ARDS, diseased alveoli may collapse during early to mid-exhalation and may open late during mid- to late inspiration.

• **At low lung volumes below lower inflection point,** cyclic opening and closure of alveolar units during tidal breathing may lead to **lung injury (damage of small airways and alveoli) from generated shear forces**.

• The most subjected regions to this type of injury are at the interface between lung units that are edematous and non-functioning, and regions that are recruitable and mildly affected by the ARDS process.

• The upper and lower inflection points are discussed above in the compliance curve.

3- Biotrauma:

• It is the release of inflammatory cytokines from neutrophils that infiltrate the lungs due to the mechanical ventilation itself (and not due to the volutrauma or barotrauma). These cytokines released in the lungs could enter the systemic circulation and travel to distant organs to produce widespread inflammatory injury and multiorgan failure as do severe sepsis and other causes of multiorgan failure.

4- Pulmonary Barotrauma:

Barotrauma occurs in 60% of ARDS patients.

Causes: Barotrauma occurs when the total lung capacity (**TLC) is exceeded** and **trans-alveolar pressure** becomes **≥ 30-35 cm H_2O** (the trans-alveolar pressure is the difference between the alveolar pressure and the pleural pressure).

Complications: Gas may escape producing:

• Pneumothorax.
• Mediastinal or subcutaneous emphysema.
• Pneumo-pericardium or pneumo-peritoneum.
• Systemic air.
• Broncho-pleural fistula.

N.B.: There are two concepts that emphasize the ventilator induced lung injury:

Open Lung Ventilation Concept:

This concept tries to adjust the end-expiratory and end-inspiratory volumes, in a patient with ARDS as follows:

• **End-expiratory volume:**

It is set at a level high enough to prevent alveolar deflation to decrease the shear forces needed to re-inflate collapsed alveoli. It is **determined clinically** at the lower inflection point of the static inspiratory pressure-volume curve of the respiratory system which is **usually at PEEP values of 2-3 cm H_2O above lower inflection point**.

• **End-inspiratory volume:**

It is set at a level low enough to prevent alveolar over-distention i.e., below the upper inflection point. It is **determined clinically** at **a peak inspiratory pressure < 20 cm H_2O above PEEP or it is limited to 35-40 cm H_2O** which is usually at tidal volume 350-400 cc.

Baby Lung Concept:

ARDS lung is considered like a baby lung with two main features:

- Decreased lung volumes.
- Decreased lung compliance.

Lung Protective Strategy (Lung Protection):

It is sometimes called **"low tidal volume strategy".**

Value:

This strategy produces an improvement in survival rates, in ARDS patients and less systemic inflammatory processes.

There is no single, agreed upon approach for protective ventilation, yet most strategies share the basic components of low tidal volume and permissive hypercapnia.

A- Protocol for Low Volume Ventilation in ARDS

Goals: • Tidal volume (Vt) = 6 mL/kg
• Inspiratory plateau pressure (Pplat) = < 30 cm H_2O

- PaO_2 = 55-80 mm Hg or SpO_2 = 88-95%
- pH = 7.30-7.45

Step 1: Adjust Vt at 6 mL/kg and Pplat at 30 cm H_2O

1- Calculate predicted body weight (PBW) in kg. it is performed either by:

- [2.3 x (height in inches – 60)] + 50 in males
  or 45.5 in females
- [0.91 x (height in cm – 152.4)] + 50 in males
  or 45.5 in females

N.B.: Predicted body weight (PBW) is the body weight at which lung volumes are normal.

2- Set initial tidal volume to 6 mL/kg PBW. (If the tidal volume is already set higher, lower it by 1 mL/kg/hour until reaching 6 mL/kg PBW).

3- When Vt down to 6 mL/kg, measure Pplat with 0.5 seconds pause every 4 hours and after every change in PEEP or Vt.

Then adjust Vt according to Pplat (the target is to reach Pplat < 30 cm H_2O).

- If Pplat is > 30 cm H_2O, decrease Vt 1 ml/kg steps until Pplat drops below 30 cm H_2O or Vt reaches 4 mL/kg PBW.
- If Pplat < 25 cm H_2O and Vt < 6 mL/kg, increase tidal volume by 1 mL/kg PBW.

Step 2: Adjust minimal both FiO_2 and PEEP to maintain PaO_2 55-80 mm Hg or SpO_2 88-95%. Choose one of the following recommended combinations:

FiO_2	PEEP cm H_2O	FiO_2	PEEP cm H_2O
0.3	5	0.7	10-14
0.4	5-8	0.8	14
0.5	8-10	0.9	14-18
0.6	10	1.0	18-24

The minimum PEEP recommended is 5 cm H_2O

Step 3: Adjust respiratory rate to keep pH at target 7.30-7.45

1- Initial respiratory rate to maintain same minute ventilation is chosen.

2- Adjust respiratory rate according to the pH of the arterial blood

- If pH < 7.15-7.30, increase respiratory rate until pH > 7.30 or respiratory rate reaches 35 (do not exceed respiratory rate > 35/min).
- If pH < 7.15, increase respiratory rate to 35/min. If pH is still < 7.15, increase Vt at 1 mL/kg increments until pH > 7.15.
- If pH > 7.45, decrease respiratory rate

B- Permissive Hypercapnia

- As a sequelae of the above ventilatory parameters (low tidal volume), hypercapnia occurs. Some authors adjust the respiratory rate to return the $PaCO_2$ to its normal values, but **in permissive hypercapnia, the respiratory rate is adjusted at low rates** to provide pulmonary rest and decreasing cyclic opening and closure of the alveoli.
- **$PaCO_2$** which is allowed to **increase up to 20-40 mm Hg above the baseline (usually up to 60-70 mm Hg) and pH is kept at 7.2-7.25**.

When pH becomes < 7.2 i.e. severe respiratory acidosis, HCO_3^- is used.

This technique is **contraindicated in** patients with **increased intracranial tension** and **cautiously used in** patients with **ischemic heart disease or severe left ventricular dysfunction.**

C- Other Considerations in Lung Protective Strategy:

1- **Low tidal volume** (6 mL/kg) is the most important parameter and the only factor proved to decrease mortality rates.

2- **Inspiratory plateau pressure (Pplat) is kept < 30 cm H_2O** or peak inspiratory pressure is kept < 20 cm H_2O above PEEP.

3- **The minimum PEEP** recommended is 5 cm H_2O i.e., above the lower inflection point on the static pressure-volume curve of the respiratory system to:

- prevent repeated opening and closure of alveoli and decrease their exposure to the large shear stress as they change from completely closed to completely open.
- allow opening of collapsed alveoli i.e., alveolar recruitment.

Avoid high PEEP, as this may - decrease venous return (causing hypotension),
- increase pulmonary vascular resistance,
and - impair ventricular performance.

4- **Liberal sedation** is used to improve patient-ventilator synchronization.

5- There are many **ventilatory modes** that can be used in lung protective strategy:

- Synchronized intermittent mandatory ventilation (SIMV).
- Pressure support ventilation.
- Biphasic positive airway pressure (BiPAP).
- Pressure controlled ventilation with a small PEEP.
- Inverse ratio ventilation.

Details of these ventilatory modes are discussed in the chapter of "Intensive (Critical) Care".

Adjuvant Ventilatory Therapy Used in ARDS Patients:

A- Prone Ventilation:

Recently, it has been found that ventilation in the prone position improves oxygenation. This usually takes several hours to occur, but when the patient returns to the supine position, desaturation occurs in minutes. This method is not used except if other methods fail to increase O_2 in the supine position. For more details, see later.

N.B.: **Recruitment maneuvers in ARDS** include:

- PEEP.
- High levels of continuous positive airway pressure (CPAP).
- Prone ventilation.

These techniques recruit collapsed lung units, allowing them to participate in oxygenation and ventilation.

B- Trans-Tracheal Gas Insufflation:

It has been tried in some ARDS patients to correct hypercapnia.

C- High Frequency Ventilation

It is discussed in chapter "Intensive Care".

D- Extra-Corporeal Membrane Oxygenator (ECMO):

Aim: It is one of the extra-pulmonary methods to supplement gas exchange. Its aim is to achieve total gas exchange or just to remove excess CO_2 only.

Indications: Patients who remain severely hypoxemic despite maximal ventilatory support and care e.g., patients with $PaO_2 < 50$ mm Hg for more than 2 hours with FiO_2 of 1.0 and conventional PEEP or patients with $PaO_2 < 50$ mm Hg for more than 12 hours with FiO_2 of more than 0.6 and conventional PEEP.

Methods:

- It consists of
  - a pump,
  - an oxygenator (bubble-membrane),
  - vascular access; which is of 2 types:
    - Veno-arterial: in which conventional ventilation is usually used.
    - Veno-venous: in which pressure-limited volume-cycled ventilation is usually used.
  - circulatory tubes that are either heparin coated or not where heparin infusion is used to maintain full anticoagulation.
- The patient should be fully sedated, paralyzed, and anticoagulated.
- ECMO is **combined with low frequency positive pressure ventilation** (respiratory rate = 4 cycles/min) with a reduced tidal volume (6 mL/kg) and peak pressure limited to 40 cm H_2O, where arterial oxygenation is achieved by continuous flow of oxygen administered via a small catheter inserted into the trachea just above the carina.

Advantages:

- It improves oxygenation and allows reduction of FiO_2.
- It allows reduction in both the airway pressure and insufflated volume; therefore, it decreases the risk of barotrauma.
- It helps to decrease hypoxic pulmonary vasoconstriction and improve right ventricular function.

ECMO does not improve the progress of the ARDS or mortality. Its clinical application for the treatment of ARDS is not appropriate or economically justified.

Complications:

1. In veno-arterial ECMO: pulmonary hypo-perfusion and bleeding may occur.

2. Thrombocytopenia, abnormal platelet function, low fibrinogen and or antithrombin III concentration may occur.

More details of ECMO are discussed in the chapter of "Cardiac Surgery".

E- Intravascular Oxygenator (*IVOX*):

Aim: It is one of the extra-pulmonary methods to supplement gas exchange. Its aim is to remove excess CO_2 mainly.

Methods:

- It is a device containing multiple hollow fibers (length 55-65 cm) consisting of an ultra-thin gas-permeable siloxane polymer membrane supported by a skeleton of microporous polypropylene. 100% O_2 flows under negative pressure (between -300 and -500 mm Hg) inside the hollow fibers. The subatmospheric intra-fiber pressure is used to avoid the risk of gas embolism in case of fiber rupture (figure 12-31).
- Insertion of the device is performed only surgically. It is inserted through a femoral venotomy and passed until the tip of the device is located in the inferior portion of the superior vena cava or within the right atrium, as determined by fluoroscopy.
- The patient should be fully sedated, and paralyzed. Full anticoagulation is needed by a continuous heparin infusion.
- Diffusional gas exchange then occurs between the subatmospheric oxygen inside the hollow fibers and blood flowing between the fibers bundle floating in the central venous blood stream, achieving continuous in vivo blood oxygenation and CO_2 extraction.
- Ventilatory mode used during IVOX: different modes can be used, but usually pressure-limited volume-cycled ventilation is used. This type of ventilatory mode usually causes hypercapnia which is removed by IVOX. It removes about 20% of CO_2 produced. CO_2 elimination is monitored by capnography. Its effect in improving oxygenation is mild and less than ECMO.

Low- frequency positive pressure ventilation is not used with IVOX due to the poor performance of IVOX as compared with ECMO.

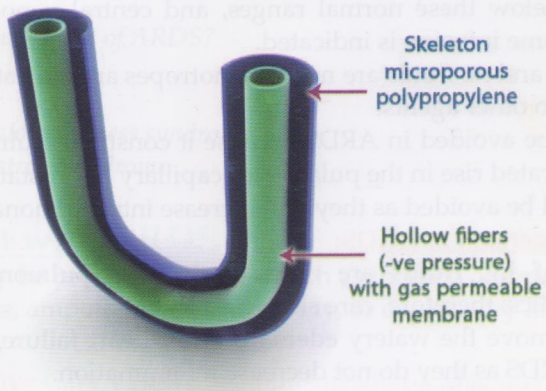


Figure 12-31: IVOX

Complications:

- Bleeding during insertion of the device.
- Thrombocytopenia.
- Infection.
- Impaired venous return due to the large size of the device.

N.B.: Extra-Pulmonary Devices to Supplement Gas Exchange include:

- ECMO.
- IVOX.

F- Liquid Ventilation:

It is the use of **perfluorocarbons (PFC)**, a substance used as an oxygen carrier, one of the artificial blood substitutes, during mechanical ventilation of patients with ARDS. The details of perfluorocarbons are discussed in the chapter of "Fluid & Electrolyte Disturbances".

Mechanism of Action:

• **Alveolar recruitment** due to the high density of PFC that decreases the alveolar and peak airway pressures.

• PFC eliminate the air-fluid interface in the surfactant deficient alveoli. This **decreases the pulmonary surface tension, improving pulmonary compliance** and decreasing the work of breathing.

• PFC allow **redistribution of pulmonary blood flow (perfusion)** when they fill the unventilated alveoli. This **decreases the intrapulmonary shunt**, improving oxygenation.

• PFC have an **anti-inflammatory action** because they have a high density which displaces the exudates filling the alveoli, inflammatory mediators, and debris up above the PFC medium; so, they can be removed easily by suctioning.

Types of Liquid Ventilation:

Total	Partial
• Both the lungs and ventilator are filled with the liquid which is pumped in and out of the lungs by using specialized devices. • It increases pulmonary vascular resistance (due to compression of pulmonary vessels) causing right ventricular overload which in turn decreases the cardiac output.	• Conventional ventilators are used to ventilate liquid filled lungs (where the functional residual capacity of the lungs is filled with liquid 30 mL/kg). PFC are re-dosed at 2-3 hour intervals due to their evaporation (under research clinically). • There is no increase in the pulmonary vascular resistance.

The use of liquid ventilation in healthy lungs is harmful due to decreased compliance and surfactant production. This decreases oxygenation.

III. Pharmacological Management:

1- Inotropes:

• The **cardiac output** should be maintained at **5-6 L/min or 3-4 L/min/m²** when adjusted for body size.

• If the cardiac output is below these normal ranges, and central venous pressure or wedge pressure is not elevated, volume infusion is indicated.

• If the cardiac output is low and no fluids are needed, inotropes are indicated.

• **Dobutamine is preferred** to other agents:

- Dopamine should be avoided in ARDS because it constricts pulmonary veins, and this will cause an exaggerated rise in the pulmonary capillary hydrostatic pressure.
- Vasodilators should be avoided as they will increase intrapulmonary shunt.

2- Diuretics and Fluid Management in ARDS:

Diuretics and restriction of i.v. fluids are used to decrease pulmonary edema. There are many disadvantages of using diuretics; therefore, care should be taken.

• Although diuretics can remove the watery edema fluid in heart failure, diuretics can not remove the inflammatory exudates in ARDS as they do not decrease inflammation.

• Aggressive diuretics may cause dehydration and decrease venous return to the heart. This can be augmented by the use of positive pressure mechanical ventilation. The decrease in venous return causes a reduction in cardiac output which in turn decreases systemic O_2 transport. Therefore, monitoring of cardiac filling pressures and cardiac output by a pulmonary artery catheter is very important in this case.

3- Corticosteroids: such as methylprednisolone 2-3 mg/kg/day.

• Although they are very potent anti-inflammatory drugs, they have no role in prevention or initial treatment of ARDS.

• They are used **in the fibrotic stage i.e., 7-14 days after** the onset of illness. They can decrease inflammation and **inhibit fibrosis** in the lungs.

4- Inhaled Nitric Oxide (NO):

Inhalation of NO in doses up to 2 parts per million (ppm) in respiratory failure can produce dose-dependent selective pulmonary vasodilatation without causing systemic vasodilatation, reduce intrapulmonary shunts and improve PaO_2.

5- Activated Protein C (*Xigris*):

It has been tried with good results in ARDS and sepsis.

More details about NO and activated protein C are discussed in the chapter of "Pharmacological Adjuncts to Anesthesia and Intensive Care".

6- Prostacyclin:
Short term infusion is used to produce pulmonary vasodilatation, so it can be used to treat pulmonary hypertension.

7- Surfactant:
The role of exogenous surfactant therapy is still being evaluated. Although it is an accepted practice in neonates, yet there are no adult studies showing long term improvement.

8- Inhaled β-Adrenergic Agonists:
They are used to treat the associated bronchospasm.

9- Antibiotics:
They are used to control infection based on culture and sensitivity.

10- Other Drugs: such as non-steroidal anti-inflammatory drugs, antioxidants, cytokine antagonists, leukotriene inhibitors are tried, but none of them has proven to be successful.

IV- Supportive Care in Intensive Care:

1- Removal of Secretions:
After adequate hydration and humidification of inspired gases, tracheal suctioning, chest physiotherapy, and postural drainage are performed. Fiberoptic bronchoscopy is used to remove thicker secretions.

2- Nutritional Support:
Nutritional support is important to prevent skeletal muscle weakness and aid diaphragmatic contraction. The caloric need should be increased while carbohydrate diet should be decreased to elevate respiratory quotient.

3- Blood Transfusion:
Some recommend to keep the hemoglobin above 10 g/dL, but blood transfusion itself may cause ARDS; therefore, if there is no evidence of tissue dysoxia or impending dysoxia (e.g., an O_2 extraction ratio ≥ 50%), there is no need to correct anemia with blood transfusion.

4- Measures to Prevent Stress Ulcer and Deep Venous Thrombosis are required.

N.B.: Infant Respiratory Distress Syndrome is discussed in the chapter of "Pediatric Diseases".

Q: Discuss recent ventilatory management of ARDS?
A: As above.
Q: What is pediatric ARDS?
A: Discuss • *Acute (adult) respiratory distress syndrome.*
• *Infant respiratory distress syndrome.*

Anesthesia for Patient with ARDS

Many patients with ARDS may be prone to surgeries such as incision and drainage of abscesses, excision of skin grafts in burned patients, amputation, tracheostomy, or exploratory laparotomy.

Anesthetic Problems:

1- Differences between Intensive Care Ventilators and Anesthetic Machine Ventilators:
ARDS patients in intensive care units are usually ventilated with intensive care ventilators which differ from anesthetic machine ventilators in many aspects. This may lead to inability of anesthetic machine ventilator to deliver the suitable respiratory parameters to ARDS patients resulting in more hypoxia and respiratory failure in these patients.

Difference between Intensive Care and Anesthetic Machine Ventilators include:

	Anesthesia Machine Ventilators	*Intensive Care Ventilators*
Inspiratory flow rate	They can only provide low gas flow rate about 50 L/min.	*They can provide higher gas flow rates up to 180 L/min.*
Peak inspiratory pressure (PIP)	They can only generate PIP up to 50-60 cm H_2O; therefore, they cannot deliver gas flow against increased airway resistance.	*They can generate PIP up to 120 cm H_2O; therefore, they can deliver gas flow against increased airway resistance.*
Tidal volume	They deliver a limited range of tidal volumes.	*They deliver a **wide range of tidal volumes** e.g., very low tidal volumes in pediatrics and in protective lung strategy in acute respiratory distress syndrome.*

Modes	Usually volume controlled mode only Recently, some types incorporate synchronized intermittent mandatory ventilation (SIMV).	*Many modes can be applied e.g., assisted control, synchronized intermittent mandatory ventilation (SIMV), pressure support, inverse ratio, pressure controlled, and biphasic positive airway pressure ventilation (BiPAP).*
PEEP	Not available, but some types can	*Available*
Delivery of anesthetic gases	*Can*	*Can not; so, anesthesia is maintained (if needed) by total intravenous anesthesia (TIVA).*

Recently, many anesthetic machines incorporate a ventilator resembling intensive care ventilators. Also other intensive care ventilators may incorporate a vaporizer to provide anesthesia for: e.g.,

- Patients with acute respiratory distress syndrome undergoing incision and drainage of abscesses.
- Burned patients with severe bronchospasm undergoing excision of skin grafts.

The use of anesthetic machine ventilators in ARDS patients may lead to:

1- Hypercapnia causing respiratory acidosis.

2- Development of auto-PEEP because the respiratory rate is increased to compensate for the decreased tidal volume.

3- Hypoxemia from decreased tidal volume.

2- Prone Ventilation:

It cannot be continued (technically difficult) intraoperatively; therefore, when the ARDS patient is turned to the supine position, rapid desaturation occurs in minutes.

3- Adjuvant Drugs: are used in ARDS patients.

- Corticosteroids:

Critically ill patients (even without a history of adrenal insufficiency) should receive a perioperative steroid cover due to increased stress.

Resistant hypotension to volume and vasopressors may be due to adrenal insufficiency.

- Activated Protein C:

It increases the risk of perioperative bleeding; therefore, its infusion should be discontinued 2 hours before surgery and at least 12 hours have to pass after surgery before restarting.

- Nitric Oxide (NO):

During anesthesia, its use causes formation of nitrogen dioxide (irritant) as NO reacts with O_2; therefore, nitrogen dioxide monitoring is essential because it is harmful.

Abrupt NO discontinuation causes an acute rebound effect; so, it should not be stopped during anesthesia. Delivery of NO during anesthesia is discussed before.

4- Volume Status:

Volume should be restricted in ARDS patients. ARDS patients cannot tolerate blood loss during surgery; therefore, monitoring of the volume status is essential and if fluid is given, gas exchange should be monitored.

5- Patient Transport:

ARDS patients need adequate FiO_2 and PEEP. This can be achieved by either:

- A valved system (Ambu-bag).
- An unvalved (Jackson Rees).

Although the minute ventilation of the patient exceeds the fresh gas flow, decreased FiO_2 in the valved system and increased $FiCO_2$ in the unvalved system occur.

6- Choice of Anesthesia:

Both i.v. and inhalational anesthetics have a little effect on oxygenation in ARDS patients.

Inhalational anesthetics in ARDS are controversial:

Advantages: - They produce rapid bi-directional titration.
- They need no i.v. route.
- They are more familiar to anesthesiologists.

Disadvantages: - They decrease alveolar epithelial fluid clearance and increase alveolar barrier permeability to proteins after oxidant-stress injury.
- They worsen oxygenation in acute lung injury.

More details are discussed in the chapter of "Intensive (Critical) Care".

Aspiration Pneumonitis

Causes of Perioperative Aspiration:

1- High ASA physical status and unconsciousness.
2- Emergency operations.
3- Difficult airway management.
4- Predisposing (risk) factors which include:
1. Upper gastrointestinal bleeding.
2. Decreased tone of the lower esophageal sphincter e.g., pregnancy, obesity, drugs, or naso-gastric tubes.
3. Gastro-esophageal reflux or esophageal strictures (for solids and not for liquids).
4. Increased volume and/or acidity of gastric contents.
5. Increased intra-gastric pressure e.g., in lithotomy position.
6. Delayed Gastric Emptying:
a- Physiological causes: pain, anxiety, and pregnancy.
b- Pathological causes:
- Acute gastro-paresis as gastroenteritis, ketoacidosis, electrolyte imbalance, hypercalcemia or migraine.
- Gastrointestinal obstruction.
- Diabetes (for solids, but not liquids).
- Polymyositis or dermatomyositis.
- Systemic sclerosis.

c- Pharmacological causes:
- Opioids.
- Anticholinergics as atropine, hyoscine, anti-histaminics, phenothiazines and tricyclic antidepressants.
- Sympathomimetics as isoprenaline and salbutamol.
- Dopamine.
- Nefopam.
- Alcohol.

7. Gastric outlet obstruction (pyloric obstruction) for solids and not for liquids except in advance cases.
8. Small or large intestinal obstruction.

N.B.: Although there is a clinical impression that obesity causes delayed gastric emptying, there has been evidence that obesity is associated with accelerated gastric emptying of liquids and solids.

Pathology of Aspiration Pneumonitis:

Injury from aspiration occurs by 3 mechanisms:

1- Mechanical obstruction by particulate matter: It causes atelectasis resulting in an intra-pulmonary shunt which increases the alveolar-arterial O_2 gradient. This causes arterial hypoxemia.

2- Chemical pneumonitis by the acidic gastric fluid (when its pH is < 2.5): It causes destruction of pneumocytes type I and II (decreasing surfactant) and capillary endothelium resulting in atelectasis. Some authors refer to this pathology as **aspiration pneumonitis.**

3- Bacterial pneumonitis by bacterial contamination. Some authors refer to this pathology as **aspiration pneumonia.**

All these mechanisms cause picture of ARDS.

Clinical Picture:

The earliest and the most reliable sign is **hypoxemia** refractory to O_2 therapy. The pulmonary consequences of aspiration depend on:

1- The volume of aspirate:

If the aspirated volume is > 25 mL (0.4 mL/kg), it causes aspiration pneumonitis.

2- The character of the aspirated material (whether solid or liquid):

Aspirated particulate (or solid) matter may cause respiratory obstruction at any level.

Patients of both groups can show:

- **Acute effects** such as immediate acute respiratory distress, cyanosis, dysrhythmias and cardiac arrest.
- **Chronic effects** that occur after 6-8 hours, with a mild chronic course of aspiration pneumonitis and lung abscess. There are stagnant secretions and bacterial infections e.g., E. coli, pseudomonas, klebsiella, anaerobes, staphylococci or bacteroids.

3- The pH of the aspirate: Aspirated material with pH < 2.5 will cause **Mendelson's Syndrome:** It is acute chemical aspiration pneumonitis, first described by Mendelson in 1946.
It is due to the irritative action of gastric HCl which causes bronchiolar spasm, and peri-bronchiolar exudates, as well as its congestive action. It is characterized by a tri-phasic sequence of clinical events:
a- A phase of immediate respiratory distress: dyspnea, tachypnea, tachycardia, cyanosis, bronchospasm, pulmonary edema, congestive heart failure up to cardiac arrest.
b- A phase of partial recovery.
c- A phase of gradual return of respiratory dysfunction: picture resembling ARDS.

Investigations:

1- Chest x-ray:

Patchy pneumonitis appears as patchy irregular densities (fluffiness or whiteout) especially in the right lower lobe. It occurs after 6-12 hours (figure 12-32).

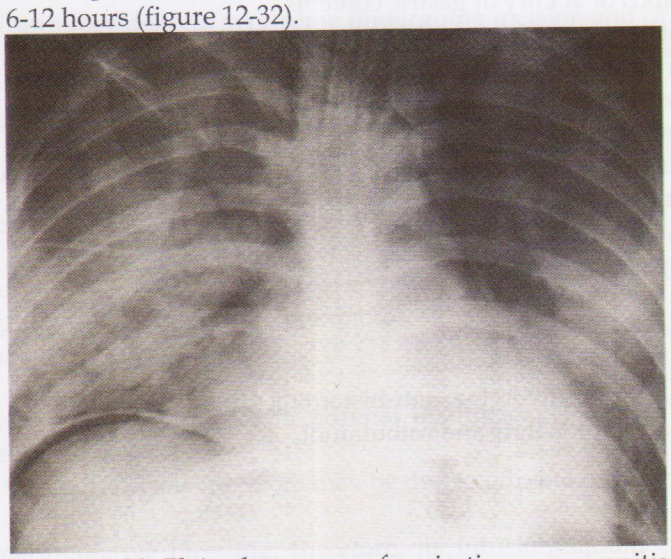


Figure 12-32: Plain chest x-ray of aspiration pneumonitis. Postoperative air under diaphragm is also noted

2- Arterial blood gas analysis: shows hypoxemia.

Management and Intensive Care Considerations:

It is better to prevent aspiration pneumonitis than to treat it.

I- Prevention:

1. Measures Decreasing Gastric Fluid Volume:

a) For Elective Surgeries: Patients should be kept **fasting preoperatively** i.e., **NPO** according to **ASA recommendations**. These recommendations are applied only to healthy patients, candidates for elective surgery. It is not applied to women in labor. These recommendations are discussed in details in chapter "The Practice Conduct of Anesthesia".
Preoperative fasting does not ensure an empty stomach. It was found that 12-80% of patients scheduled for an elective surgery have a gastric volume of > 0.4 mL/kg and a pH of < 2.5.

b) For Emergency Surgery:
The stomach should be emptied by either:
- physical means as a large bore **naso-gastric tube** which is withdrawn before induction of general anesthesia.
- pharmacological means: such as
  - **metoclopramide** (*Plasil*): 10 mg i.v/i.m 1-2 hours before induction of general anesthesia.
  - **cimetidine:** 300 mg i.v/i.m 1-2 hours before induction of general anesthesia.

or - ranitidine: 50 mg i.v/150 mg i.m 1-2 hours before induction of general anesthesia.

The best guidelines are as follows:
1- Elective surgery should be postponed till 6 hours after ingestion of solid food.
2- **One cup of clear fluids is permitted and encouraged 2 hours before surgery.**
3- Metoclopramide, H_2 blockers, antacids and antiemetics are administered only to patients at increased risk of aspiration. They are not used routinely as studies have showed no decrease in the incidence of aspiration with or without them.

2. Measures Decreasing Gastric Acidity:

a. Neutralize the Existing Acid: by **non-particulate antacids** e.g., Na citrate (15-30 mL of 0.3 molar solution 15-30 minutes before induction of general anesthesia) or $NaHCO_3$.

Advantages:

- Effective in reducing hydrogen ions concentration of gastric contents for about 30 minutes.
- Na citrate (unlike $NaHCO_3$) does not produce CO_2 in the stomach; therefore, it does not interfere with capnography as a diagnostic aid to tracheal versus esophageal intubation.
- Non-particulate antacids are more preferred than particulate antacids such as magnesium tri-silicate or aluminum hydroxide as particulate antacids mix poorly with gastric contents and if they are aspirated, they cause pneumonitis.

b. Suppress New Gastric Acid Secretion: by H_2-receptor antagonists such as cimetidine or ranitidine. They increase the gastric pH to > 2.5 in 80% of patients.

No single agent or combination has been shown to give optimum intra-gastric conditions indicative of complete protection.

3. Measures Preventing Regurgitation:

a. Increase the Tone of the Lower Esophageal Sphincter: by

- Metoclopramide.
- **Avoiding drugs that decrease the tone of the sphincter** e.g., atropine, opioids, benzodiazepines before induction of anesthesia.

b. Avoid Increased Intra-Gastric Pressure: by

- Avoiding positive pressure ventilation before intubation.
- **Precurarization**: Pretreatment with a small dose of non-depolarizing muscle relaxant 5 minutes before suxamethonium, to prevent fasciculations that increase intragastric pressure. Recently, it has been shown that fasciculations do not increase the risk of regurgitation because suxamethonium increases the lower esophageal pressure than the intragastric pressure; therefore, it increases barrier pressure, which protects against aspiration.

4. Measures Preventing Aspiration if Regurgitation occurs:

a. **Rapid-sequence induction (crash induction).**

b. Induction in **the lateral position with a head down tilt.**

c. **Cricoid pressure (Sellick's maneuver):** It is applied from the beginning of induction till inflation of the cuff of an endotracheal tube. The efficacy and safety of cricoid pressure have been questioned in some researches by some authors, but it is the most important by other authors. Cricoid pressure maneuver should be avoided if the patient is actively vomiting because there is risk of esophageal rupture.

d. Presence of **powerful suction machine**.

e. Usage of **cuffed endotracheal tubes.**

5. Awareness of Intubation Difficulties.

6. Usage of Awake Intubation.

7. Regional Anesthesia.

II - Treatment:

If aspiration of gastric contents occurs, the following measures must be carried out immediately:

1. Position: **Lateral position with head down tilt** (to 30 degrees) must be carried out immediately to have the larynx at a higher level than the pharynx and to allow gastric contents to drain to the outside.

2. Oro-Pharyngeal Suctioning: It is done under vision by a laryngoscope.

3. Prompt Endotracheal Intubation with a Cuffed Endotracheal Tube: to prevent further aspiration.

4. Suction through the Inserted Endotracheal Tube:

This should be done before administration of 100% O_2 by positive pressure ventilation to prevent further pushing of the aspirated material beyond reach. **Suction** should be **brief** to avoid cardiac arrest from hypoxemia. **Tracheo-bronchial aspirate** should be collected for **culture and sensitivity** tests. **O_2 100%** should be given after suction.

Tracheo-Bronchial Lavage Role:

- **If the aspirate is mainly an acid aspirate, avoid bronchial irrigation with $NaHCO_3$, NaOH, or normal saline** as this will aggravate the pulmonary lesion because:
  - The large volume of fluid will push HCl acid deeper into lungs.
  - Neutralization the HCl acid with $NaHCO_3$ produces heat and thermal injury of the bronchial mucosa.
  - HCl acid causes damage within a very short period of time, so the treatment will not be effective.

- Mixing of HCl acid with the treatment solution is often impossible due to the minute size of interface.
- If equal volumes of HCl acid with a pH of 1.6 and $NaHCO_3$ are mixed, the pH increases only to 1.8.

• **If the aspirate is mainly particulate matter with obstruction, bronchial irrigation may be performed with normal saline**; 5-10 mL are instilled into the tracheo-bronchial tree followed immediately by suction. It should be preceded and followed by oxygenation. The sequence should be repeated till the suction fluid is clear.

5. Bronchoscopy: is indicated if particulate matter is present in the aspirate or if there are signs of obstructive atelectasis. Tracheo-bronchial lavage with a large volume of saline is no longer recommended.

6. Supplemental O_2 Therapy and Continuous Positive Airway Pressure (CPAP).

7. Ventilatory Support: such as synchronized intermittent mandatory ventilation (SIMV) with PEEP and pressure support.

8. Restoration of the Intravascular Volume: is recommended especially by **albumin solutions** because hypoalbuminemia occurs due to extravasation of protein containing fluid into the lungs.

9. Bronchodilators: are needed to relieve bronchospasm.

10. Corticosteroids:

Such as - Methyl prednisolone 30 mg/kg i.v.
or - Dexamethasone 0.1 mg/kg i.v.

Their uses are controversial.

Advantages:

1. They decrease the inflammatory process.
2. They decrease pulmonary cellular damage and protect type II alveolar pneumocytes by stabilization of lysosomal membranes.
3. They decrease agglutination of platelets and leukocytes.
4. They decrease pulmonary H_2O content.

However, the effectiveness of corticosteroids is related to the pH of the aspirate:

• If the pH of the aspirate is in the narrow range of 1.5-2.5, corticosteroids may be effective.
• If the pH of the aspirate is < 1.5, pulmonary parenchymal damage is maximal and corticosteroids are ineffective.
• If the pH of the aspirate is > 2.5, the effect is like that of distilled water; therefore, corticosteroids are not needed.

Disadvantages:

1. They decrease resistance to infection. There have been some reports of increased gram-negative pneumonia after steroids.
2. They interfere with normal healing processes.

Therefore, steroids are not used routinely for patients with gastric acid aspiration pneumonitis.

11. Prophylactic Antibiotics:

They do not improve mortality or decrease secondary infection rates. Drug-resistant bacterial and fungal super-infection may develop.

Indications: Only used with:

1. Signs of infection: fever, leukocytosis, positive cultures (the initial aspirate, excluding feculent aspirate, is usually sterile and remains so for the first 24 hours).
2. Possibility of intestinal obstruction:

Antibiotics (penicillin + aminoglycosides) may be administered without waiting for evidence of pulmonary infection. They can be discontinued if there is no clinical or laboratory evidence of infection.

12. Monitoring and Further Investigations:

• Measurement of the **gastric fluid pH** is useful because it reflects the pH of the aspirated fluid, while measurement of the tracheal aspirate pH is of doubtful value because inhaled gastric fluid is likely to be rapidly diluted by airway secretions.
• Frequent **arterial blood gases analysis** should be performed.
• **Hemodynamic monitoring:**
  ▫ Arterial line: for continuous invasive arterial blood pressure monitoring.
  ▫ Pulmonary artery catheter: for measurement of pulmonary capillary wedge pressure, cardiac output, pulmonary vascular resistance, and systemic vascular resistance.

Other Forms of Non-Cardiogenic Pulmonary Edema

	Neurogenic Pulmonary Edema	High Altitude Pulmonary Edema	Negative Pressure (Post-Obstructive) Pulmonary Edema	Drug-Induced Pulmonary Edema	Reexpansion Pulmonary Edema
Cause	**Acute brain injury** especially in the area of the medulla produces severe **sympathetic stimulation** which results in generalized **vaso-constriction. This** shifts blood volume from the systemic to the pulmonary circulation causing pulmonary edema usually after hours from brain injury.	**High altitudes** (> 2400 m or 8000 Ft) cause sustained alveolar hypoxia. This results in **hypoxic pulmonary vaso-constriction** which increases the pulmonary vascular pressure producing pulmonary edema.	**Vigorous inspiratory efforts against acute upper airway obstruction** or a closed glottis e.g., laryngospasm, obstructive sleep apnea, or epiglottitis produce **high negative intra-pleural pressure.** This high negative intra-pleural pressure causes: • a decrease in the interstitial hydrostatic pressure. • an increase in the venous return and left ventricular load. • intense sympathetic activation, hypertension and central displacement of blood volume. These effects increase the trans-capillary pressure gradient which causes **transudation** and movement of fluid out of the pulmonary circulation **into the alveoli (Müller maneuver).** Then on **sudden relief of the obstruction**, pulmonary edema becomes apparent.	After administration of an overdosage of a number of drugs especially **opioids (heroin) and cocaine.** Cocaine may also cause pulmonary vaso-constriction which increases pulmonary edema.	Rapid re-expansion of a collapsed lung may lead to pulmonary edema in that lung e.g., after relief of pneumo-thorax or pleural effusion. If the amount of air or liquid is > 1 liter and the duration of collapse is > 24 hours, the risk of pulmonary edema increases.
Treatment	• Decreasing intracranial tension. • Diuretics should not be used unless there is hypervolemia because development of hypovolemic hypotension could aggravate the central nervous system insult. • $O_2 \pm$ PEEP. • Mechanical ventilation.	• Descend to near sea level. • $O_2 \pm$ PEEP. • Nifedipine: It causes pulmonary vasodilatation; so, it is used as a prophylactic measure in susceptible patients. • A portable hyperbaric chamber (Gamow bag) can be used for rapid simulation of descent.	• It usually resolves spontaneously. • Diuretics • $O_2 \pm$ PEEP • Mechanical ventilation.	• Supportive measures. • Diuretics • $O_2 \pm$ PEEP • Mechanical ventilation. There is no evidence that naloxone speeds resolution of opioid-induced pulmonary edema.	• Supportive measures.

Lateral Decubitus (Unilateral) Pulmonary Edema:

It occurs when the patient lies in lateral decubitus where fluids pool into the dependent lung due to the effect of gravity.

Sarcoidosis

It is a systemic granulomatous disease involving many tissues especially:

- **Thoracic lymph nodes**. It needs mediastinoscopy for diagnosis.
- Lung: **Chronic intrinsic restrictive lung disease and corpulmonale**.
- **Laryngeal sarcoid**: It interferes with passage of an adult size tracheal tube.

- Parotid gland, facial nerve and optic nerve involvement.
- Myocardial sarcoidosis: **heart block, dysrhythmias or restrictive cardiomyopathy.**
- **Hepatic granuloma and splenomegaly.**
- **Fever** of unknown cause.
- **Hypercalcemia.**

Treatment: Corticosteroids.

Disorders of the Pleura and Mediastinum

I. Pneumothorax

Definition: Presence of gas within the pleural space.

Causes:

a. Spontaneous (primary):
- Idiopathic.
- Congenital bullae.
- Marfan's syndrome.
- Generalized emphysema.
- Bronchial asthma.
- Rapid decompression of divers.

b. Traumatic:
- External penetrating chest injury causing disruption of the parietal pleura.
- A tear in lung parenchyma causing disruption of the visceral pleura.
- Rib-fracture.

c. Iatrogenic:
- Cervical or thoracic surgery.
- Brachial plexus blockade.
- Cannulation of subclavian or internal jugular veins.
- Inadvertent barotrauma.

Clinical Picture: Ipsilateral collapse of the lung causing ventilation/perfusion mismatching:
- It may be asymptomatic.
- There may be sudden severe chest pain, dyspnea, asymmetric chest expansion and hyper-resonance on percussion of the chest.

During Anesthesia, there may be:
- Decreased or absent breath sounds.
- Unexplained bronchospasm and altered pattern of breathing.
- Unexplained tachycardia and hypotension.
- Arterial hypoxemia causing cyanosis and sudden decrease in the pulse oximetry reading.

Investigations:

1- Plain chest x-ray, before induction of anesthesia is important if there is chest trauma. Pneumothorax is most easily seen in erect views with the following signs:
- Hyperlucent lung field compared to the contralateral side.
- Loss of clarity of the diaphragm outline.
- Deep sulcus sign giving the appearance of an inverted diaphragm.
- Clear cardiac contour.

2- Ultrasound.

3- CT scan: is very sensitive especially in difficult situations as ARDS and to direct drainage of a localized pneumothorax (figure 12-33).

Management:
- Spontaneous pneumothorax (asymptomatic as < 20% of lung has collapsed): It **spontaneously resolves**, but O_2 only may be needed.
- **N_2O should be stopped and 100% O_2 with positive pressure ventilation is needed** immediately.
- **Chest tube with underwater seal** in the **4th or 5th intercostal space** anterior to **the mid-axillary line** is usually inserted. It **may be** inserted under **ultrasound or CT guidance** if a localized pneumothorax is present due to surrounding lung fibrosis.
- In recurrent cases, **chemical pleurodesis** (without thoracotomy) is done by instilling **tetracycline** into the pleural space.

• An air leak from the lung that persists for > 7-10 days after chest tube insertion may indicate a major bronchus injury that needs **surgical intervention**.

Tension Pneumothorax

Definition:

It develops when gas enters the pleural space during inspiration and is prevented from escaping during expiration. This one way valve like-action causes a progressive increase in the amount of air trapped under increasing pressure (tension).

Causes: The same as pneumothorax.

Clinical Picture: is the same as pneumothorax, but:

• It is more severe up to obstructive **shock** (with congested neck veins).

• It is associated with **mediastinal compression** with tracheal shift to the normal side.

Treatment:

Emergency treatment: Needle aspiration or i.v. cannula (gauge 14, 3-6 cm long) insertion in the **mid-clavicular line into the 2nd intercostal space** with underwater seal to relieve tension. It converts tension pneumothorax to open pneumothorax, and then **chest tube placement** is inserted as above.

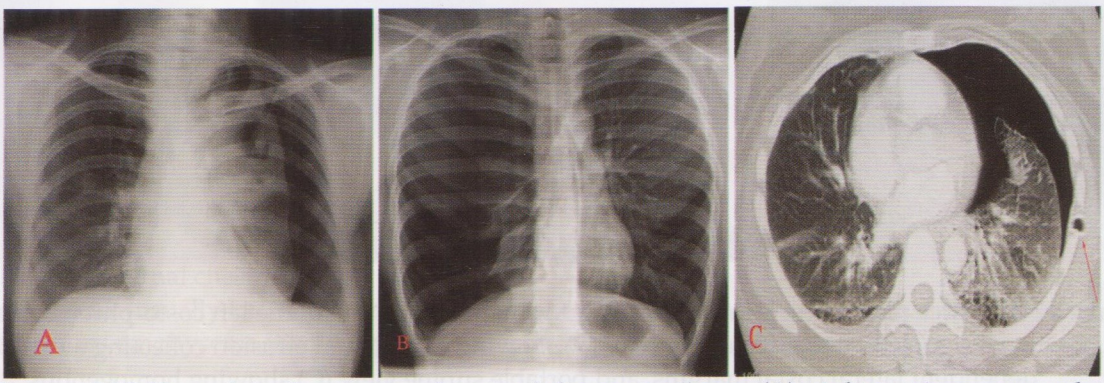


Figure 12-33: Two plain chest x-rays showing left pneumothorax (A), right tension pneumothorax (B) with shifting of the mediastinum and complete lung collapse. CT chest (C) showing left pneumothorax(air appears jet black) due to open chest trauma (arrow).

II- Pleural Effusion

Definition: It is an abnormal collection of fluid in the pleural space.

Normally there is a small amount of fluid present in the pleural space that functions to mechanically couple the lung to the chest wall and lubricate the interface of the visceral and parietal pleura.

Causes:

a- An exudative pleural effusion: There is **a disease** process that is **affecting the pleura** directly causing damage of the pleura and/or its vasculature.

• Local disease in pleural space such as **malignancy** (14%).

• Local disease adjacent to pleural space such as **pneumonia** (22%), **pulmonary embolism** (11%), **and sub-diaphragmatic abscess**.

• Systemic diseases that affect the pleural surface such as **autoimmune diseases (lupus and rheumatoid arthritis)**.

b- **A transudative pleural effusion:** The **pleura** itself is **healthy and intact**, but a remote disease process affects hydrostatic and/or oncotic pleural pressure such as **congestive heart failure** (36%) **and myxedema**.

Clinical Picture:

• Clinical picture of the cause may be present as fever and productive cough that may indicate pneumonia.

• Chest pain, particularly when sharp and made worse with breathing, can result from an inflammed pleura in the presence of effusion.

• Dyspnea and hypoxia as the effusion can affect the mechanics of the diaphragm and cause compressive atelectasis and result in restrictive lung disease.

• Dullness over effusion detected by percussion.

• Decreased breath sounds detected by auscultation.

Investigations:

1- Plain chest x-ray:

• **Posterior-anterior (PA) chest x-ray** shows blunting of the costo-phrenic angle and a meniscus sign (the most common findings when an effusion is present). It is less sensitive as it can detect effusions of more than 500 mL of fluid.

• **Lateral decubitus chest x-ray** (where the dependent side is the side of the effusion) shows the fluid as a straight line between the chest wall and the lower border of the lung. It is the most sensitive view as it can detect as little as 175 mL of fluid.

• **A portable chest x-ray while the patient lies supine** in the bed (it is the most commonly performed in intensive care patients) shows increased basilar opacity with graduation over the entire hemithorax (more opaque at the base than the apex). It is the least sensitive view. It does not show either obliteration of the costo-phrenic angle or the meniscus sign (figure 12-34).

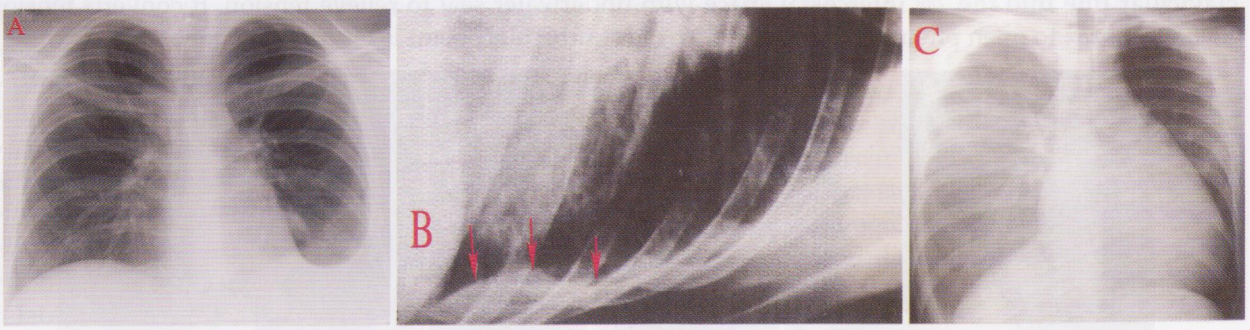


Figure 12-34: Three plain chest x-rays; PA view (A) showing blunting of the left costo-phrenic angle and meniscus sign, left lateral decubitus view (B) showing free pleural effusion collecting along the dependent lateral costal margins, and portable supine view (C) showing homogenous increased density of the right hemithorax

2- Chest computed tomography (CT): is very sensitive to diagnose and quantify the amount of effusion, but it needs patient's transportation which is sometimes very difficult in intensive care patients. It includes:

• **Noncontrast CT scans** that give an idea about the amount of effusion and can detect abnormalities in the lungs that can be obscured by the effusion on standard chest x-ray.

• **Standard contrast CT scans** that also give an idea about the pleural surfaces such as presence of pleural malignancy (figure 12-35).

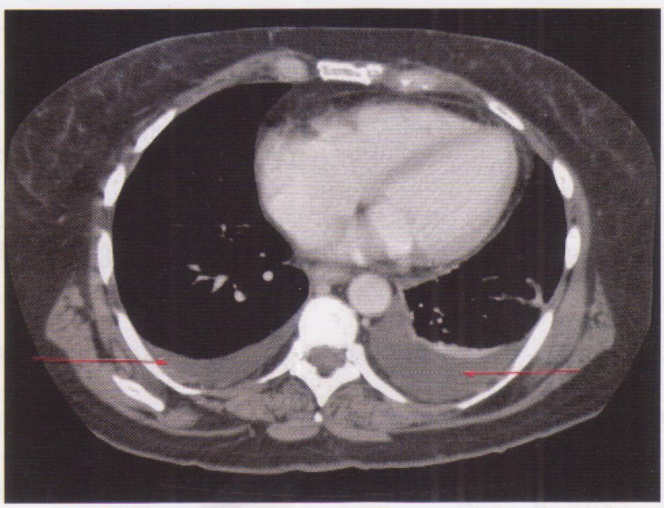


Figure 12-35: Contrast enhanced CT scan of the chest showing bilateral pleural effusion (arrows)

3- Ultrasound: can detect the localized or free-flowing effusion. It is a bedside investigation that can also be used as a guide for thoracocentesis or thoracotomy tube insertion.

4- **Thoracocentesis** is performed to obtain **a sample of the effusion for analysis** especially if the fluid layer is more than 1 cm in lateral view chest x-ray. It is helpful to differentiate between exudative and transudative pleural effusion. Exudative pleural effusion is characterized by the following criteria:

- Light's criteria: - Pleural fluid to serum protein ratio is > 0.5
  - Pleural fluid to serum lactate dehydrogenase (LDH) ratio is > 0.6
  - Pleural fluid LDH > 2/3 upper limit of normal for serum LDH.
- Heffner's criteria: - Pleural fluid protein > 2.9 g/dL.
  - Pleural fluid LDH is > 0.45 upper limit of normal.

Management:

- Treatment of the cause if possible e.g., antibiotics in case of pneumonia.
- Intercostal tube insertion may be needed.
- In cases of severe hemothorax (presence of blood in the pleural space), blood transfusion may be required.

III. Pneumo-Mediastinum

Definition: It is presence of air/gas inside the mediastinum.

Causes:

1- Spontaneous (idiopathic).
2- After tracheostomy.
3- After alveolar rupture.

Clinical Picture:

- Sudden retro-sternal chest pain, and dyspnea.
- Pneumothorax (usually left) can occur due to passage of gas into the pleural space.
- Subcutaneous emphysema involving the neck, arms, abdomen and scrotum.

Treatment:

- Spontaneous cases usually resolve without treatment.
- Rarely, surgical decompression is needed if it compresses vascular structures.

IV. Mediastinal Mass

Causes:

- Retro-sternal goiter.
- Tumors as lymphomas, thymomas, or teratomas.

Preoperative Management:

1- Preoperative assessment of causes.
2- Preoperative assessment of clinical picture.

Mediastinal masses may cause compression of:

a. The Airway (and Trachea): causing airway obstruction which worsens by lying supine.
This airway obstruction is due to - direct mechanical compression
or - mucosal edema by superior vena cava syndrome.
Proximal obstruction causes dyspnea.
Distal obstruction causes dry cough.
Therefore, **preoperative assessment of the airway** e.g., chest X-ray, CT scan, and flow-volume loops are mandatory.

b. Superior Vena Cava (SVC): leading to **SVC syndrome** with obstruction of venous drainage from the upper 1/2 of the body (which worsens in the supine position). This results in:

- Edema and venous congestion of the face, neck, upper chest and conjunctiva.
- Edema of the hypo-pharynx; so, difficult intubation should be suspected.
- Edema of the upper limbs; so, i.v. line and central line are preferred in the legs.
- Evidence of increased intracranial tension as headache, and decreased mentality.
- A Valsalva effect (which decreases venous return) may be associated with syncopal events.

c. Lung: leading to a **restrictive lung disease**.

d. Pulmonary Artery and Heart: leading to **hypoxemia and hypotension** (decreased cardiac output due to decreased venous return to the heart and SVC compression) especially on anesthesia.

3. At least one large bore i.v. cannula should be placed in the lower limb because venous drainage from the upper limb is unreliable and it is life-saving in case of injury of one of the tributaries of SVC during surgery.

4. Preoperative chemotherapy: may cause complications such as lung fibrosis.

5. Preoperative radiotherapy: may cause difficult airway management.

6. Premedication is better avoided.

Intraoperative Management:

Monitoring: Standard monitors are essential besides invasive arterial blood pressure monitor.

Choice of anesthesia:

a. Local anesthesia:

It is the safest especially for biopsy from a peripheral lymph node (cervical or scalene).

b. General anesthesia:

- It is usually indicated for young and uncooperative patients.
- **Awake intubation** is preferred in cooperative patients with or without fiberoptic laryngoscope.
- **Inhalational induction** by halothane or sevoflurane then intubation for uncooperative patients can be used as an alternative.
- A helium (70%) and oxygen (30%) (*Heliox*) mixture may be used to improve oxygenation in patients with airway compression. Heliox has one third the density of oxygen, permitting more laminar gas flow and decreasing resistance in the conducting airways.
- If the patient deteriorates during induction, turning him or her in the left lateral decubitus position may improve cardio-respiratory function.
- **An armored endotracheal tube** should be used. It must **bypass the obstruction of the airway.** Extra long endotracheal tubes in small sizes should be available to pass through fixed narrow airways.
- **Avoid coughing and straining** as they may increase the positive pleural pressure resulting in increased intra-thoracic pressure. This precipitates complete airway obstruction; therefore, the armored tube **should pass the area of compression**.
- Patient **hemodynamics** should be maintained.
- Mechanical ventilation can cause **severe hypotension**; therefore, volume loading is needed.
- At the end of surgery, the patient is left intubated **until the airway obstruction is resolved.** This is determined by - the flexible bronchoscope.
  - Air leak around the endotracheal tube on deflation of its cuff.
- Recovery room personnel must be notified of the effect of position on the patient's cardio-respiratory status as lateral or prone decubitus position may relief airway obstruction.

Other Pulmonary Diseases

I. Bronchial Carcinoma:

Anesthetic Problems:

- Patients usually have - **Chronic bronchitis.**
  - **Infection and lung collapse** distal to the tumor.
- Patients may have **myasthenic syndrome**.
- Para-malignant syndrome (in Oat cell carcinoma) with secretion of many hormones especially:
  - Antidiuretic hormone (ADH): Syndrome of inappropriate ADH secretion causing dilutional hyponatremia.
  - Adreno-corticotropic stimulating hormone (ACTH): Cushing syndrome.

II. Pulmonary Tuberculosis:

Anesthetic Problems:

- It affects lung function either **the cavitary syndrome, restrictive lung disease**.....etc.
- If the disease is active, all anesthetic equipment should be **sterilized** after usage to avoid cross-infection and it is better to use antibacterial filter between the patient and the anesthetic machines or the tubing circuits of intensive care ventilators.

Pulmonary Embolism

Definition:

It is entry of a blood clot, fat, tumor cells, air, amniotic fluid or any foreign materials (insoluble material) into the venous system.

Causes:

I. Venous thrombo-embolism: It mostly occurs in awake patients.
II. Venous air embolism: It mostly occurs in anesthetized patients.
III. Fat embolism.
IV. Amniotic fluid embolism.

I. Venous Thrombo-Embolism (VTE):

A- Superficial Thrombophlebitis:

It occurs after i.v. drug injection or infusion especially etomidate, or diazepam. The vein appears as a cordlike structure surrounded by an area of erythema, warmth, and edema.
Fever may be present, if there is bacterial infection. It very rarely produces pulmonary embolism.

Management:

a. Thrombo-prophylaxis:
- Use infusions > i.v. injections.
- Change the site every 12 hours.
- Use a cannula formed from poly-tetra-fluor-ethylene (Teflon).

b. Active treatment:
- Elevate the affected site.
- Apply local heat over the affected sites.
- Give antibiotics if bacterial infection is suspected.

B- Deep Vein Thrombosis (DVT):

Most DVT are initiated by platelet adhesion either to endothelial tissue or to exposed collagen of damaged vascular walls. As platelet aggregation continues, the clot becomes organized and begins to trap circulating white and red blood cells. Deposition of fibrin organizes the clot and allows it to build a stable matrix.
An embolus is a fragment of the thrombus that breaks off and travels in the blood until it lodges at a site of vascular narrowing. An embolus originating in a vein commonly lodges in the pulmonary vasculature.

Etiology and Risk Factors

Risk factors are simplified as **Virchow's Triad** for DVT (in the deep venous system of the lower limbs or the pelvis) which includes:
- **Venous stasis.**
- **Vessel wall (endothelial) damage.**
- **Hypercoagulable status.**

Risk Factors are classified According to their Risk as Follows:

Risk Factors (1 Point Each):

- Age 41-60 years.
- Central line.
- General anesthesia time > 2 hours.
- Hyperviscosity syndromes.
- Laparoscopic surgery.
- Immobilization > 12 hours.
- Estrogen therapy (oral contraceptive pills).
- Family history of DVT or pulmonary embolism.
- Inflammatory bowel diseases.
- Stroke with paralysis.
- Low cardiac output as myocardial infarction, congestive heart failure, hypovolemia, hypotension, or hypothermia.
- Leg swelling, ulcers, stasis (a tourniquet, head up position), varicose veins.
- Previous history of operative DVT.
- Pregnancy or < 1 month postpartum.
- Obesity (> 20% over ideal body weight or body mass index > 30).

N.B.: Some researches ignore that obesity per se is not a proven risk factor for DVT.

Risk Factors (2 Points Each):

- Age 61-70 years.
- Multiple trauma.
- Previous history of idiopathic DVT.
- Major surgery.
- Malignancy (Trousseau syndrome).
- Spinal cord injury with paralysis.

Risk Factors (3 Points Each):

- Age > 70 years.
- Acquired thrombophilia.

• Previous history of pulmonary embolism.
• Inherited thrombophilia as factor V Leiden which resists activated protein C, prothrombin variant mutations causing increased prothrombin levels, anticardiolipin, dys-fibrinogenemia, antibody syndrome, antithrombin III deficiency, protein C or protein S deficiency, hyperhemo-cysteinemia, and myelo-proliferative disorders.

Total Risk Factor Score

Low risk = 0
Moderate risk = 1-2
High risk = 3-4
Very high risk = > 4

Thromboembolic Risk Stratification for Surgery Patients

Low Risk Patients:

The incidence without prophylaxis; of DVT is 0.4-2%, of symptomatic pulmonary embolism is 0.2%, of fatal pulmonary embolism 0.002%.

• Uncomplicated surgery in patients < 40 years of age with minimal immobility postoperatively and no risk factors.
• Surgical time < 60 minutes.
• Pregnancy.

Moderate Risk Patients:

The incidence without prophylaxis; of DVT is 2-40%, symptomatic pulmonary embolism is 1-8%, of fatal pulmonary embolism is 0.1-0.4%.

• Any surgery in patients aged 40-60 years.
• Major surgery in patients > 40 years of age and no other risk factors.
• Minor surgery in patients with 1 or more risk factors.
• Surgical time > 60 minutes.
• Myocardial infarction postpartum, especially with previous DVT; estrogen use; varicose veins.

High Risk Patients:

• Surgery in patients aged > 60 years.
• Major surgery in patients aged 40-60 years with one or more risk factors.

Very High Risk Patients:

The incidence without prophylaxis; of DVT is 10-80%, of symptomatic pulmonary embolism is 5-10%, of fatal pulmonary embolism is 1-5%.

• Major surgery in patients > 40 years of age with previous venous thromboembolism, cancer, or known hypercoagulable state.
• Major orthopedic surgery.
• Elective neurosurgery, multiple trauma, or acute spinal cord injury.
• Stroke, paraplegia, prolonged bed rest, burns, obesity, or hypercoagulable state.

Clinical Picture:

a. Clinical Picture of DVT:

• Throbbing pain, edema, skeletal muscle (calf muscles) spasm in DVT affecting the veins of the lower limbs or pelvis. Tenderness induced by compression of the calf muscles anteriorly against the interosseous membrane or with passive dorsiflexion of the ankle (Homans' sign) is present in less than 30% of patients.
• Nearly always above knee DVT is the one, which produces pulmonary embolism, while below knee DVT or arm thromboses very rarely produces pulmonary embolism, but generally most of these thromboses are subclinical and resolve completely when mobility is restored.

b. Clinical Picture of Pulmonary Embolism:

According to the size of venous emboli reaching the lung:

1. **Acute massive pulmonary embolism**:

It involves > 50% of the main pulmonary artery causing obstruction of pulmonary artery outflow. It produces:

• Sudden dyspnea and tachypnea up to irregular gasping respiration.
• Sudden circulatory collapse and death.

2. **Chronic showering of pulmonary micro-emboli:** It produces:

• Pulmonary infarctions with episodes of pleuritic chest pain and hemoptysis.
• Chronic thrombo-embolic pulmonary hypertension.

• In the elderly, multiple small pulmonary emboli may be misdiagnosed as broncho-pneumonia.

The most common time for presentation of pulmonary embolism is **postoperatively** especially during **the 2nd week**.

During Anesthesia:

• Unexplained sinus tachycardia, cardiac arrhythmias, hypotension up to circulatory collapse and sudden death in massive pulmonary embolism.

• Bronchospasm.

• Unexplained arterial hypoxemia (decreased PaO_2) causing central cyanosis, an acute decrease in $PaCO_2$, decreased $ETCO_2$ (and increased $P\bar{v}CO_2$), and increased alveolar-to-arterial difference for CO_2.

• Increased jugular venous pressure.

• Appearance of the 4th heart sound on heart auscultation.

Investigations:

a. For DVT:

1. Duplex ultrasound: is the most common investigation done nowadays. B-mode ultrasonography with vein compression is also very sensitive (preferable than venography or impedance plethysmography).
2. Fibrinogen uptake test:

A radio-labeled fibrinogen is injected before the operation and then a scan is done to detect incorporation of fibrinogen into the newly formed thrombus non-invasively.

Both are used as screening tests.

3. Impedance plethysmography: relies on changes in electrical resistance associated with alteration in limb volume. DVT impedes venous outflow and causes a slower change in impedance when a proximally occluding cuff is deflated. It is not a highly specific test.
4. CT scanning and MR venography show a filling defect.
5. Contrast venography is the gold standard invasive technique, which shows a filling defect or abrupt termination of the dye column.

b. For Pulmonary Embolism:

1. Electrocardiography (ECG): shows tachycardia and signs of right ventricular strain.

• Right axis deviation.
• Right bundle branch block.
• Inverted T wave in leads $V_1 - V_4$.
• P pulmonale.
• The classical S_1-Q_3-T_3 is less common (figure 12-36): A large S wave in lead I, a Q wave in lead III, and an inverted T wave in lead III indicate acute right heart strain. This pattern only occurs in about 10% of people with pulmonary embolism.

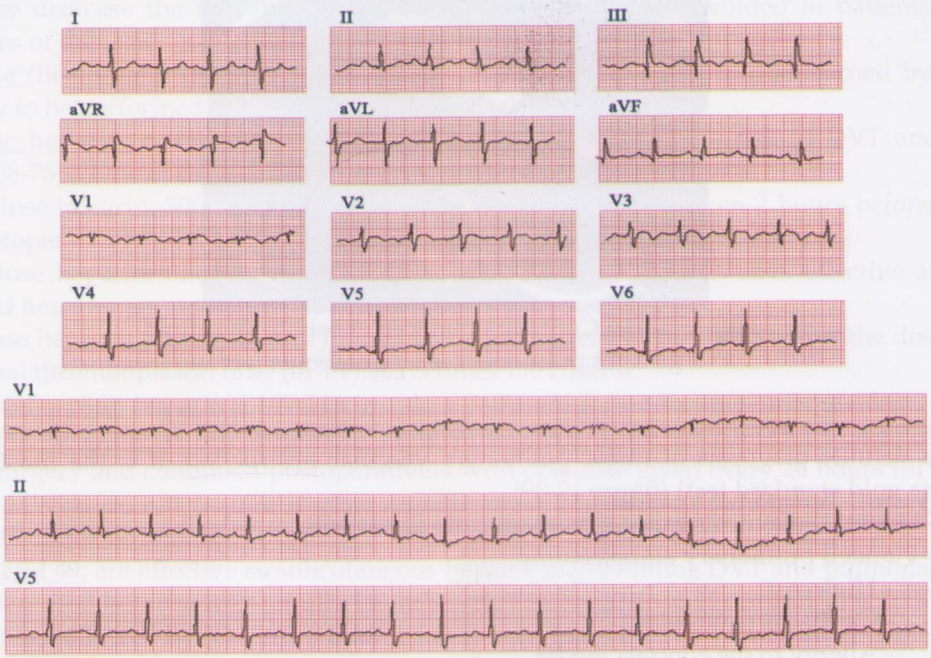


Figure 12-36: ECG of pulmonary embolism showing the classical S1-Q3-T3, sinus tachycardia, inverted T waves in V1-V4

2. Chest X-ray:

It is sensitive in 45% of patients; chest x-ray is normal initially. Changes occur **after 2 days** from the event.

Chest x-ray shows:

- Pulmonary oligemia (radiolucency) due to pulmonary vascular obstruction.
- Pulmonary infarction (wedge shaped density).
- Pulmonary atelectasis.
- Pulmonary hypertension with enlarged proximal pulmonary artery.

3. Arterial Blood Gases:

- Decreased PaO_2 due to increased alveolar dead space.
- Decreased $PaCO_2$ due to hyperventilation.

4. Perfusion and Ventilation Lung Scans:

- Perfusion scan: A sensitive test shows uneven circulation with perfusion defects (figure 12-37).
- Ventilation scan: It is usually normal.

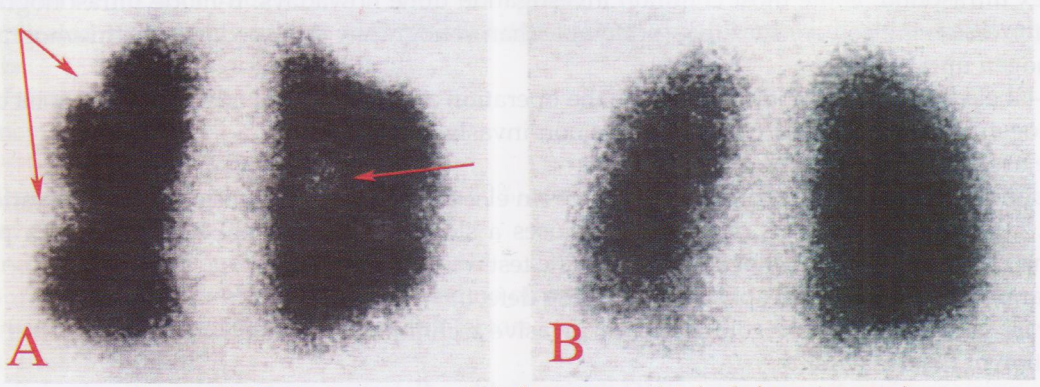


Figure 12-37: Perfusion scan (A) showing multiple defects (arrows) with normal ventilation scan (B) denoting pulmonary embolism

5. Spiral computed tomography (CT) scan of the chest (figure 12-38) with contrast:

It can detect the emboli

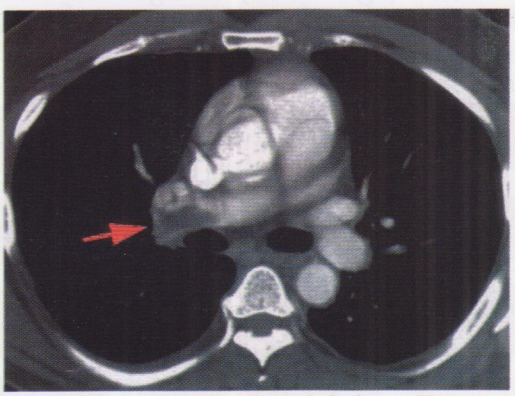


Figure 12-38: Contrast-enhanced chest CT revealing a large right pulmonary artery embolus (arrow)

6. Pulmonary Angiography (Arteriography):

It provides a definite diagnosis of major pulmonary vascular obstruction. It is **the most sensitive and specific test (a gold standard test)** (figure 12-39).

Indications: - Doubtful diagnosis especially in critically ill patients.
- Planned pulmonary embolectomy.

Disadvantages: - High cost.
- Cardiac arrhythmias.
- Allergy to the contrast media.

Therefore, it is not used routinely.

Recently, **Digital subtraction arteriography** replaces the need for direct pulmonary injection of contrast media, but it is injected intravenously through a catheter into the pulmonary artery (figure 12-39).

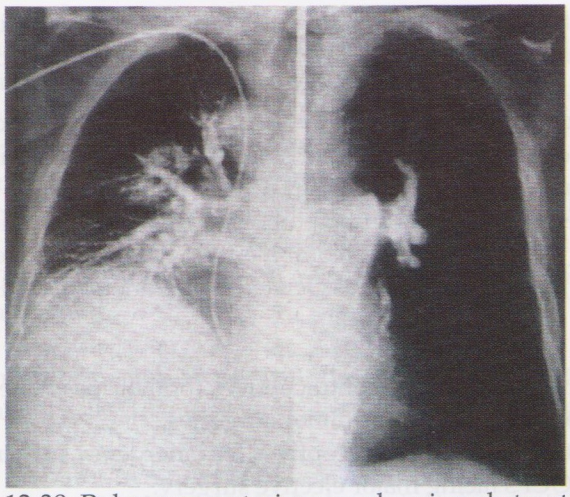


Figure 12-39: Pulmonary arteriogram showing obstructions of many of the large branches of the left pulmonary artery

7. Trans-Esophageal or Precordial Echocardiography:

It shows - acute dilation of the right atrium and right ventricle.
- pulmonary hypertension.
- a thrombus that may be apparent in the main pulmonary arteries.

8. D-Dimer Test:

A **positive test** means that a venous thrombosis or a **pulmonary embolism is possible**, but a **negative test strongly suggests that thrombo-embolism is absent** (a negative test predictive value is >99%). Plasma D-dimer is a degradation product of plasmin digestion of mature cross-linked fibrin.

Management:

A) Thrombo-Prophylaxis:

I) Preoperative Prophylaxis: (in high-risk patients).

1. Correction of **risk factors** whenever possible.
2. **Adequate hydration.**
3. Graded leg compression **elastic stockings** (either below-the-knee or more preferable above-the knee stocking): They decrease the incidence of DVT 44%. They should be avoided in patients with severe arterial diseases of the legs.
4. **Leg exercise** (flexion and extension of the knees, ankles and feet) should be learned by the patients preoperatively to be performed by patients postoperatively.
5. Prophylactic **heparin**: is the most effective method in decreasing the risk of DVT and pulmonary embolism by 68-76%. One of the following methods can be used:

• Usual low-dose heparin: 5000 IU subcutaneously every 8-12 hours; given 2 hours before surgery and continued postoperatively till the patient is ambulatory.

• Ultra-low dose heparin: one IU/kg/hour i.v. infusion. This method is safe, effective and decreases discomfort and hematomas associated with the subcutaneous route.

• Adjusted dose heparin: start with 3500 IU subcutaneously every 8 hours and adjust the dose to keep the activated partial thromboplastin time (aPTT) at 1.5 times the control.

• Low molecular weight heparin (LMWH): in a dose 3400 anti-factor Xa units or equivalent. For example: enoxaparin (2000 or 40 mg) cortoparin (3000), dalteparin (2500), or tinzaparin (3500). One dose is given 12 hours before surgery and continued postoperatively with one dose given every 24 hours till the patient is ambulatory. LMWHs do not require routine monitoring of coagulation parameters during its use. It is effective as subcutaneous heparin.

6. **Dextran 70 and 40:** are effective as subcutaneous heparin in preventing DVT and pulmonary embolism, but are not often used because they require i.v. infusion. The usual dose of dextran 40 is 100-200 mL as an intravenous bolus followed by 30-40 mL/h for 2-3 days after surgery. They act by coating platelet surfaces to reduce adhesion. They also increase plasma volume and decrease the viscosity of blood.

7. **Aspirin**: provides some protection against venous thrombo-embolism, but it is less than subcutaneous heparin.

8. **Warfarin**: in a fixed low dose (2 mg/day) or as a monitored dose (target international normalized ratio "INR" 2.0-3.0) for 2 weeks preoperatively, and then as a higher monitored dose after the operation.

9. **Fondaparinux:** is an indirect factor Xa inhibitor. It acts by potentiating the anti-factor Xa activity of antithrombin. Fondaparinux has no effect on routine coagulation studies, and monitoring is not necessary. The usual dose is 2.5 mg given subcutaneously and started 6-8 hours after surgery.

10. **Recommendations for oral contraceptive pills (OCPs):**

OCPs increase the risk of perioperative thrombo-embolism by up to 3-4 times especially third generation pills containing desogestrel or gestodene (i.e. combined OCPs). Progestogen only OCPs (and injectable progestogen contraceptives) have not been associated with an increased risk of DVT or pulmonary embolism.

Recommendations:

- There is no need to stop progestogen only contraceptives (oral or injectable) at the time of any surgery.
- There is no need to stop combined OCPs for minor surgeries.
- There is no possibility of stopping any contraceptives for emergency surgery.
- For patients on combined OCPs facing major elective surgery:
  - Manufacturers recommend stoppage for 4 weeks before major surgery and restarting only after the menstrual period by at least 2 weeks following full mobilization.
  - Other authors recommend taking a decision on an individual basis, balancing the risk of thrombo-embolism, the possibility of unwanted pregnancy, and the preferences of the patient.
  - Patients receiving combined OCPs facing an intermediate or major surgery should receive subcutaneous LMWH and wear anti-embolism stocking.
  - If the combined OCPs are stopped, advice must be given about alternative contraceptive measures, and a pregnancy test may be needed before operation if there is a possibility of unprotected intercourse.

II) Intraoperative Prophylaxis:

a. Decreasing Venous Stasis in the Lower Limbs by:

- **Raising the legs**.
- **Avoiding leg trauma**.
- **Electrical calf muscle stimulation.**
- **Intermittent pneumatic leg compression devices**: that are effective as subcutaneous heparin in preventing DVT. They compress the leg (35-40 mm Hg) for about 10 seconds every minute, promoting venous flow.
- **Foot pumps** are similar, and promote blood flow by compressing the venous plexuses of the feet.

b. Good Anesthetic and Surgical Techniques by:

- **Adequate fluid therapy**.
- **Decreasing heat loss**.
- **Decreasing times of tourniquets**.
- **Extradural or subarachnoid block**: that is associated with **lower incidence of venous thrombo-embolism** in the early postoperative period due to the following causes:
  - **Vasodilatation** increases venous blood flow.
  - **Good postoperative analgesia allows early ambulation.**
  - **Excess fluids** decrease blood viscosity.
  - **Local anesthetics decrease platelet aggregation.**
  - General anesthesia decreases blood flow in the lower limbs by 50%.

If the patient receives prophylactic heparin, care should be taken during regional techniques.

III) Postoperative Prophylaxis: **Early ambulation** is mandatory.

B) Active Treatment:

I) Treatment of DVT: by anticoagulation therapy.

1. Heparin:

5000 IU i.v. bolus followed by 24 000-40 000 IU 24 hours infusion continued for 5-7 days. Adjust the dose to keep APTT 1.5 -2 times the normal.

In a patient who develops heparin induced thrombocytopenia, agratroban or lepirudin has to be used as alternative drugs.

N.B.: Low molecular weight heparin such as enoxaparin or dalteparin can be used in higher doses as follows; 100 anti-Xa units/kg for twice-daily administration or 150-200 anti-Xa unit/Kg for once-daily administration. It can be given for an outpatient at home.

2. Oral anticoagulants:
Warfarin is the most commonly used. It is initiated within 24 hours of heparin therapy. Heparin is discontinued when the oral anticoagulant has achieved its therapeutic effect and the oral anticoagulant is continued for at least 3-6 months or longer. The dose should be adjusted to keep prothrombin time with an international normalized ratio between 2-3 times the normal.
Care is taken that: - they are not used during pregnancy.
- cimetidine, aspirin, and 3rd generation cephalosporins potentiate warfarin.

II) Treatment of Pulmonary Thromboembolism: (due to venous thrombosis)

1. Oxygenation: from 100% O_2 up to controlled mechanical ventilation and PEEP.
2. Intravascular volume expansion.
3. Bronchodilators.
4. Circulatory support by inotropes: such as digoxin, dopamine, or dobutamine. Isoproterenol may be used as it decreases the pulmonary vascular resistance; therefore, it is preferred.
5. Anticoagulation:
a. Heparin:
5000-10000 IU i.v. bolus followed by 24 000-40 000 IU 24 hours infusion continued for 5-7 days.
Adjust the dose to keep APTT 2-3 times the normal control or the activated clotting time (ACT) 1.5-2.5 times the normal.
b. Oral anticoagulants: should be started as early as possible and continued for at least 6 months.
6. Thrombolytics such as **streptokinase:** are used in massive pulmonary embolism not responding to the above measures. The risk of hemorrhage with these agents is considerably higher than that with heparin.
7. Pulmonary embolectomy: Open pulmonary embolectomy under cardiopulmonary bypass is considered if cardiovascular effects of the embolism are life-threatening.
8. Inferior vena cava umbrella filter: A stainless steel filter is placed percutaneously under local anesthesia with fluoroscopy to prevent recurrent pulmonary embolism.

Q: Discuss hypercoagulable states?
A: They include: • *Venous hypercoagulability: It is discussed above.*
• *Arterial thrombosis: It is discussed in the chapter of "Blood Diseases".*

II. Venous Air Embolism (VAE)

Etiology:

• It occurs when a vein in which, the pressure is sub-atmospheric, is opened to the atmosphere.
• This is most likely to occur with surgical sites above the level of the right atrium such as head and neck operations in the head-up position e.g., posterior fossa craniotomy in the sitting position especially when the surgeon is dissecting tissues that do not allow veins to collapse despite a negative pressure within them.

Pathology:

Effects of VAE depend on:
1. The Total Volume of Air that entered the Circulation and the Rate of Air Entry into the Circulation:
a. Small air bubbles or low entry rates (< 0.5 mL/kg/min): cause insignificant effects and the air bubbles are dissipated by the lungs.
b. Large total volume or high entry rate (> 0.5 mL/kg/min): may overcome the ability of the lungs to dissipate air producing clinical signs such as:
• Air in the right atrium or right ventricle produces **the classical Mill wheel murmur** due to turbulence of blood.
• Air in pulmonary vasculatures causes pulmonary vascular occlusion by:
1. Mechanical obstruction by the air.
2. Humoral obstruction due to release of prostaglandins that cause severe pulmonary vasoconstriction.
This produces:
▫ Pulmonary edema and reflex broncho-constriction.
▫ An increased alveolar dead space which causes ventilation/perfusion mismatching. This decreases gas exchange which causes arterial hypoxemia and decreases CO_2 excretion, end-tidal CO_2 and expiratory PCO_2.
▫ Loss of surfactant in the area affected within hours, with subsequent atelectasis within 24–48 hours.

- Increased pulmonary artery pressure, central venous pressure and decreased cardiac output and arterial blood pressure.
- Cardiac arrhythmias.

c. Large total volume and rapid entry rate:

This causes acute right ventricular outflow tract obstruction (as it interferes with pumping of the right heart. This leads to acute right sided heart failure resulting in cardiovascular collapse and death.

2. Paradoxical Air Embolism:

It can occur due to:

- Presence of patent foramen ovale which is present in 10-25% of the population (asymptomatic).
- Presence of thebesian veins in the heart and bronchial vessels which drain in the left side of the heart.

Air may enter the systemic circulation and then, enter the coronary or cerebral arteries.

Therefore, even small air bubbles in i.v. lines and syringes should be avoided in all patients.

Clinical Picture:

It usually occurs intraoperatively. The same clinical picture as that of venous pulmonary embolism occurs in addition to:

- Sudden attempts by patients to initiate spontaneous breaths (gasp reflex) during controlled mechanical ventilation of the lungs may be the first indicator of venous air embolism.
- A **loud precordial Mill wheel murmur** (a late sign of catastrophic venous air embolism).

Monitoring: (intraoperatively)

1- Electroencephalography (ECG) shows arrhythmias.

2- Capnography shows a **sudden decrease** in end-tidal CO_2 and expiratory PCO_2. These changes occur early before occurrence of cardiovascular changes. It is the most useful monitor.

3- Pulse oximetry shows decreased SaO_2 due to decreased gas exchange and decreased cardiac output and tissue perfusion.

4- Precordial or esophageal stethoscope is the least sensitive in detection of the Mill wheel murmur.

5- Pulmonary artery pressure and central venous pressure: are increased with significant VAE. They are more sensitive than auscultation, but less sensitive than other measures and also occur late.

6- Invasive arterial blood pressure monitoring: detects hypotension which is variable.

7- Precordial Doppler ultrasound: is placed over the right 4th intercostal space.

Advantages:

- It is the most sensitive non-invasive investigation; it can detect even a small amount of air in the right atrium. Its ability to detect turbulence caused by venous air embolism can be assessed by rapidly injecting 5-10 mL of saline peripherally and listening for the characteristic change in sound quality.
- It permits continuous monitoring of the heart sounds and murmurs.

Disadvantages:

- It is affected by diathermy; so, it is difficult to detect changes while diathermy is being used. The period of the greatest risk of VAE is during opening and closing the wound and unfortunately, these are the times when surgical diathermy is most likely to be used.
- It is not quantitative and does not differentiate between a massive air embolism and a physiologically insignificant air embolism.

8- Trans-esophageal echocardiography (the method of choice):

Advantages:

- It is the most sensitive.
- It can determine the amount of air.
- It can detect small air in the right atrium, visualize the cardiac chambers and detect paradoxical air embolism.

Disadvantages:

- It is invasive.
- It needs expertise to interpret.
- It is often impossible to be performed in the horizontal operating positions.

9- Mass spectrometry (for Detection of End-Tidal Nitrogen):

There is an increase in the end-tidal N_2 which often precedes decreased end-tidal CO_2.

Advantages: It is the most specific (for presence of air), noninvasive, and quantitative test.

Disadvantage: It can be difficult to be interpreted if an-oxygen mix is being used in the anesthetic.

Management

It is better to prevent VAE than to treat it.

A) Prevention:

The aim is to keep small positive pressure in the veins at the operative site by:

1. **Proper positioning of the patient** to always maintain small positive pressure in the veins at the operative site.
2. **Expansion of the intravascular volume.**
3. **Controlled ventilation with PEEP:** that is **controversial** because:

- The clinical values of PEEP are ineffective in increasing the venous pressure significantly.
- PEEP can increase right atrial pressure towards or above the left atrial pressure. This increases the risk of paradoxical air embolism.

B) Treatment:

When VAE is detected or suspected intraoperatively, the following measures should be done:

1. **Measures to prevent further air entry:**

Notify the surgeon so that he can - identify the open vein and close it.
- flood the surgical field with saline and cover it with wet gauze.

2. **Measures to increase venous pressure at the operative site:** especially in head and neck surgeries by:
   - lowering the operative site when possible.
   - applying manual compression of the jugular veins at the neck upon the surgeon's request, bilaterally and intermittently.
3. **A Measure to avoid expansion of air bubbles:** Stopping N_2O if it has been used.
4. **Aspiration of air bubbles:** This is done through either:

- A central venous catheter with its tip **located at the junction of the superior vena cave and right atrium near the sino-atrial (SA) node** (the most efficacious method), best if the patient is placed in the left lateral position (with the right chest uppermost) to trap air in the right atrium. **Position of the catheter is confirmed by ECG guidance** where the catheter is filled with $NaHCO_3$ (to increase electrical conductance) and the right arm lead is attached to a conductive connector placed on the catheter line (i.e., forming a catheter lead). The catheter is first advanced into the right ventricle where right atrial pressure waveform is detected; then the catheter is withdrawn back until it becomes at mid-atrium where the P wave on the catheter lead becomes biphasic, and then the catheter is withdrawn back further to the point at which the P wave and QRS complex are of equal amplitude. The catheter is then pulled back another centimeter and secured.
- A pulmonary artery catheter which is not effective due to the small caliber of its lumen.

5. **Circulatory support** by:

- Expansion of the intravascular volume.
- Inotropic support such as dopamine or dobutamine.
- Vasopressor support.
- External cardiac massage.

6. **Hyperbaric oxygen therapy** may be useful in the treatment of both severe venous as well as paradoxical air embolism to decrease the size of air bubbles. It should be applied within 8 hours of the onset of symptoms.
7. **Finally, right thoracotomy:** is done to aspirate air from the right heart and to perform internal cardiac massage.

III. Fat Embolism

Although some degree of fat embolism probably occurs in all cases of long-bone fracture, fat embolism syndrome is less frequent, but potentially fatal (10-20% mortality).

In 1862, Zenker first described fat embolism at autopsy. In 1873, von Bergmann clinically diagnosed fat embolism syndrome for the first time.

Causes:

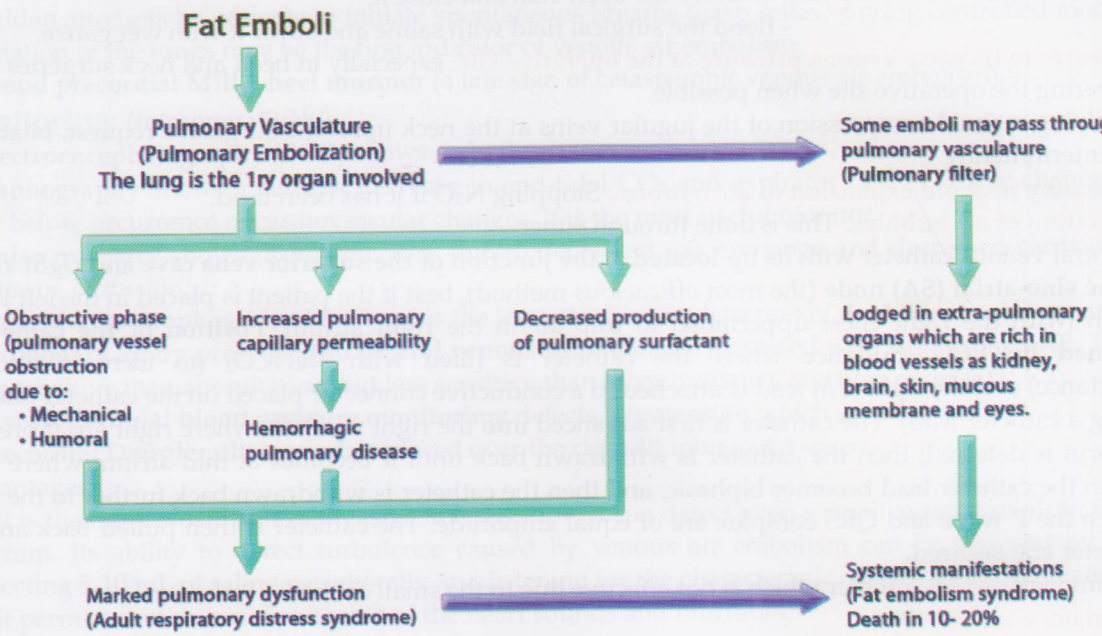
1- **Long bone or pelvic bone fractures** containing fatty marrow. Fat embolism syndrome occurs after **12-72 hours**. This is sometimes called **lucid interval**.

2- **Orthopedic surgeries** such as:

• Total hip replacement: after insertion of freshly prepared bone cement into the femoral canal. An increase in the pressure within the bone marrow cavity may occur resulting in rupture of small venules; therefore, fat globules may enter the circulation.
• Open reduction and internal fixation of hip fractures.
3- Extensive damage to subcutaneous fat deposits e.g., **liposuction**.
4- **Acute pancreatitis, cardiopulmonary bypass, parenteral infusion of lipid, or bone marrow harvest** may be associated with fat embolism syndrome.

Pathology:

There are two theories:
a- Disruption of fat cells in the fractured bone releases fat globules; the latter enter the circulation via tears in the medullary vessels (the most popular theory).
b- Changes in fatty acid metabolism cause aggregation of circulatory free fatty acids, which results in formation of fat globules in the form of chylomicrons.
The pathological changes are discussed in figure 12-40.



N.B.: Liver and pituitary glands are protected by their portal systems; therefore, they are rarely affected.

Figure 12-40: Pathological changes of fat embolism

Systemic manifestations are classified according to the severity by **Sevitt classification** into:
1. Fulminant form:
It is characterized by rapid onset of **coma and death**.
2. Classic form:
It is characterized by moderate to severe cerebral and pulmonary dysfunction, in addition to other characteristic constitutional signs.
3. Incomplete form:
It is characterized by either cerebral dysfunction or pulmonary dysfunction.

Clinical Picture: **Fat embolism syndrome** may occur **within 72 hours** after long bone or pelvic fracture with a **triad of dyspnea (and hypoxia), confusion, and petechiae**.

1. Fever: Most of the patients are febrile with a temperature as high as 41-42 °C.
2. Cardiovascular Manifestations:
• Tachycardia. • Fullness of superficial veins (due to increased venous pressure).
• Hypotension. • Acute heart failure may occur.
3. Pulmonary Manifestations: (the 1st organ affected).
• Dyspnea and tachypnea.

- Cyanosis and hypoxemia (with PaO_2 < 60 mm Hg).
- Bubbly crepitations and blood-tinged frothy tracheo-bronchial secretions.
- ARDS (with bilateral pulmonary infiltrates) may occur due to the toxic effects of elevated levels of free fatty acids on the alveolo-capillary membrane.

4. Systemic Manifestations:

a. **Renal** impairment (the 2nd organ affected).

b. **Cerebral** affections: due to damage of cerebral capillaries causing cerebral edema. Confusion, disorientation, agitation, delirium, acute psychosis, convulsions, and coma may occur. Local weakness, spasticity, decerebrate rigidity may occur also. Incontinence is common.

c. **Skin** (the classical finding): shows **petichial hemorrhages** in the capillary plexus of the dermis in a distinctive pattern over the shoulders, neck, chest, and axillae in 50% of patients.

d. **Mucous membranes** show petichial hemorrhages in the palate.

e. **Eyes:** show subconjunctival petichial hemorrhages. Emboli may appear within the retinal vessels. Streaks of hemorrhage are present throughout the retina. Macular edema usually occurs.

Gurd and Wilson Criteria for Diagnosis of Fat Embolism Syndrome:

Major Criteria	Minor Criteria
Petechiae in a vest distribution	Tachycardia > 110 beats/minutes
Hypoxemia with PaO_2 < 60 mm Hg	Pyrexia > 38.5°C
Central nervous system depression disproportionate to hypoxemia	Emboli visible in retina
Pulmonary edema	Fat in urine or sputum
	Unexplained drop in hematocrit or platelet count
	Increasing erythrocyte sedimentation rate

Investigations:

1- Complete Blood Picture: shows

- A sudden decrease of hemoglobin due to hemorrhage in pulmonary parenchyma.
- Thrombocytopenia and other coagulation test abnormalities due to disseminated intravascular coagulopathy (DIC).

2- Chest X-ray: shows

- Unevenly distributed areas of radio-density.
- Increased broncho-vascular markings and congestive hilar shadows.
- Dilatation of the right side of the heart.

3- Electrocardiography (ECG): shows

- Myocardial ischemia as depressed ST segment and inverted T wave.
- Right ventricular strain as a prominent S in lead I and prominent Q in lead III ($S_1Q_3T_3$), Right axis deviation, and right bundle branch block.
- Cardiac arrhythmias.

4- Arterial Blood Gas Analysis: shows arterial hypoxemia.

5- Serum Lipase Level:

It is non specific because it can occur after any trauma without fat embolism. It increases in 50% of cases of fat embolism. It reaches a maximum on the 7th to 8th day, but bears no relationship to disease severity.

6. Detection of Fat in:

a- Urine: (lipuria): It is non specific because it can occur after any trauma without fat embolism. It occurs in the 1st few days. It is usually associated with a severe degree of fat embolism.

b- Blood.

c- Tissues such as sputum and retina. Biopsies of petichiea and frozen sections may be helpful. Needle biopsy of the kidney to demonstrate fat globules is diagnostic.

N.B.: Criteria of bad prognosis:

- Sevitt classification.
- Serum lipase.
- Lipuria.
- ARDS.

Diagnosis during Anesthesia:

- A decline in end-tidal CO_2 and arterial saturation.
- A rise in pulmonary artery pressures.
- ECG changes.

Management:

A) Prophylaxis:

Gentle handling of the patient, immobilization of long bone fractures, and early splinting of long bone fractures are mandatory.

B) Treatment:

1. **Resuscitative measures** to correct shock.
2. **Pulmonary support:** if ARDS occurs.
   - O_2 therapy.
   - Mechanical ventilation, positive end expiratory pressure (PEEP), or continuous positive airway pressure (CPAP).
   - Rapid digitalization.
   - Endotracheal tube suction to decrease secretions.
3. **Cerebral manifestations are treated** by sedatives and anticonvulsive therapies.
4. **Corticosteroids** are of doubtful values, such as i.v. hydrocortisone 100 mg/6 hours. They may decrease the incidence of fat embolism syndrome by limiting the endothelial damage caused by free fatty acids.
5. **Low dose heparin** (not in anticoagulant doses).
   2500 IU/6 hours i.v. It clears lipemic plasma and stimulates lipase activity.
6. **Low molecular weight dextran:** is given intravenously to counteract intravascular thrombosis when there is an increase in erythrocyte sedimentation rate.
7. **Ethyl alcohol** is tried in some researches.

IV. Amniotic Fluid Embolism

It is discussed in chapter of "Obstetric Anesthesia".

Intraoperative Pulmonary Embolism:

1. **Gas Embolism (Air/CO_2/N_2O).**
   - CO_2/N_2O embolism usually occur during insufflation procedures such as:
     - Laparoscopy. - Hysteroscopy. - Arthroscopy.
   - Air embolism can occur with:
     - Head and neck surgery as sinus or mastoid surgeries.
     - Orthopedic surgery as arthroscopic, hip and spine surgeries.
     - Chest surgery as breast or open heart surgeries.
     - Others as intravascular cannulas (venous/arterial) or epidural injections.
2. **Fat Embolism:** during orthopedic surgery.
3. **Venous Embolism:** Surgical manipulation in the pelvis may dislodge a venous thrombus which is already present.
4. **Tumor Embolism:** Surgical manipulations of tumors with intravascular extension.
5. **Amniotic Fluid Embolism.**

Acute Respiratory Failure

Definition:

It is inability of the lung to provide adequate arterial oxygenation with/without adequate CO_2 elimination.

It causes • **PaO_2 to be < 50-60 mm Hg** in presence of O_2 supplementation.
• **$PaCO_2$ to be > 45-50 mm Hg** in absence of respiratory compensation of metabolic alkalosis.

N.B.:

- If metabolic acidosis is associated with respiratory failure, $PaCO_2$ is decreased below 45 mm Hg to compensate for the decrease in HCO_3^- although respiratory failure is present.
- The pH of arterial blood can distinguish between acute and chronic respiratory failure as follows:

- In acute respiratory failure, there may be an abrupt increase in $PaCO_2$ causing decreased pH.
- In chronic respiratory failure, there is a slow increase in $PaCO_2$ causing normal pH (between 7.35–7.45) due to compensatory renal tubular reabsorption of HCO_3^-.

Pontoppidan's Classification:

This classification uses values of PaO_2 and $PaCO_2$ to determine the type of respiratory failure. It is a theoretical concept and not useful in clinical practice.

	Type I (Lung Pathology)	Type II (Ventilatory Pump Failure or Hypoventilation)
Other names	**Hypoxemic Respiratory Failure**	**Hypoxemic and Hypercapnic Respiratory Failure**
Definition	• Decreased PaO_2 + normal or decreased $PaCO_2$	• Decreased PaO_2 and increased $PaCO_2$
Causes	It is due to lung pathology in airways, alveolar spaces, interstitium, and pulmonary vessels. This can occur in: 1- Obstructive lung disease such as severe acute asthma. 2- Restrictive lung disease such as • Acute intrinsic (pulmonary edema; cardiogenic or non cardiogenic) • Chronic intrinsic (severe pulmonary fibrosis).	It is due to decreased ventilatory pump or hypoventilation. This can occur in: 1- Obstructive lung disease such as severe acute asthma or severe COPD. 2- Restrictive lung disease such as chronic extrinsic due to neuromuscular disease, or morbid obesity. 3- Hypoventilation such as that due to overdose of respiratory depressant drugs. **Other causes of hypoventilation** are discussed in chapter "Problems with anesthesia".
It is not used clinically because	Many patients with type I respiratory failure, due to acute lung injury develop fatigue of respiratory muscles. This causes hypercapnia (unless they are mechanically ventilated) and they become type II respiratory failure patients.	Many patients with type II respiratory failure e.g., due to neuron disease may develop acute chest infection before complete respiratory muscle paralysis occurs; so, they will present with type I respiratory failure.

Treatment and Intensive Care Considerations:

1. O_2 Supplementation:

The aim: is to maintain the PaO_2 between 60-80 mm Hg.

There is no value or benefit from maintaining PaO_2 >80 mm Hg because Hb saturation is nearly 100% at this level and also to avoid O_2 toxicity.

FiO_2: - It should not exceed 0.5 (50% inspired O_2) for > 24 hours to avoid **pulmonary O_2 toxicity.**

- If ordinary methods (Venturi, face mask, nasal catheter) can not maintain PaO_2 >60 mm Hg with FiO_2 at 0.5, administration of CPAP or PEEP is required.
- **Patients dependent on the hypoxic drive** may show respiratory depression by O_2; so, FiO_2 should be titrated gradually with monitoring of $PaCO_2$. If $PaCO_2$ increases, assisted ventilation is required.

Methods of O_2 administration: are discussed in the chapter of "Pharmacology of Anesthesia & Intensive Care".

2. Mechanical Ventilation:

It is discussed in more details in the chapter of "Intensive (Critical) Care".

Many modes and strategies are used for example, **protective lung strategy in ARDS patients**.

3. Pharmacological Treatment: such as nitric oxide, surfactant, bronchodilators, antibiotics...etc. They are discussed in details in management of COPD and ARDS.

4. Optimization of Intravascular Volume:

Intravascular volume is monitored by:

- **Urine output**: It should be 0.5-1 mL/kg/hour.
- **Body weight**: It should be reduced by 0.2-0.4 kg/day. If the body weight is stable or increased, it indicates excessive fluid retention.
- **Central venous pressure (CVP)**: It is probably not a reliable guide for i.v. volume.
- **Pulmonary capillary wedge pressure (PCWP)**: It should be 15 mm Hg (> 15 mm Hg indicates excessive i.v. volume and < 15 mm Hg indicates inadequate i.v. volume).

If there is excessive accumulated fluid in the lung, use drug induced diuresis e.g., furosemide or dopamine (care is taken for their side effects).

5. Cardiovascular Support:

Inotropes and vasopressors may be indicated.

6. Removal of Secretions:

- Adequate systemic hydration.
- Humidification of inspired gases.
- Tracheo-bronchial suctioning of secretions.

- Chest physiotherapy.
- Bronchoscopic removal of inspissated secretions.

7. Nutritional Support:

Value: • To improve skeletal muscle power.

• To provide phosphate and magnesium. Both are essential for normal muscle power.

Muscle weakness may cause failure of weaning from the ventilator although no longer respiratory failure is present.

Caloric intake: It should be increased during respiratory failure due to the associated increased metabolism and CO_2 production; therefore, it requires increasing alveolar ventilation.

Type of caloric intake: carbohydrate intake should be restricted because it is associated with more CO_2 production.

8. Prophylaxis against Stress Ulcer:

These patients are susceptible to gastrointestinal bleeding from stress ulcers. Antacids or H_2 receptor blockers should be administered.

9. Prophylaxis against DVT:

These patients are liable for DVT due to prolonged recumbency; therefore, precautions should be taken.

Prone Position and Prone Ventilation of the Lungs

Mechanisms Improving the Arterial Oxygenation in Prone Position Ventilation:

I) Lung Volumes:

Prone position ventilation increases functional residual capacity (FRC), overall lung volumes and lung recruitment.

II) Respiratory Mechanics:

Prone position ventilation decreases chest wall compliance without change in lung compliance. The greater the reduction of chest wall compliance is, the greater the improvement in arterial oxygenation.

The chest wall compliance consists of the sum of:

- The ventral chest wall compliance.
- The dorsal chest wall compliance.
- Diaphragmatic compliance.

The dorsal chest wall, for anatomical reasons, is stiffer than the ventral chest wall and it is likely that diaphragmatic compliance does not change from the supine to the prone position. Thus the reduction of chest wall compliance in the prone position is most probably due to a decrease in the ventral chest wall compliance i.e., the ventral chest wall is stiffer in prone ventilation due to its limited range of movement because of lying against the mattress surface.

III) Regional Lung Inflation:

a- In the Supine Position:

• Regional lung inflation depends on the local trans-pulmonary pressure (defined as the difference between alveolar and pleural pressure).

Trans-pulmonary pressure = alveolar pressure - pleural pressure.

Increased trans-pulmonary pressure causes increased regional lung inflation.

• In acute lung injury/adult respiratory distress syndrome (ALI/ARDS), there is a vertical gradient of lung inflation, with the ventral regions, located near the sternum **(i.e., non-dependent) being more inflated than the dorsal regions**, located near the vertebrae (i.e., dependent). In the dorsal regions, the pleural pressure is higher and trans-pulmonary pressure is lower compared with the ventral regions.

Several factors affect the pleural pressure gradient and consequently, regional lung inflation in the supine position:

- **The superimposed pressure on the lung:** In ALI-ARDS patients, the superimposed pressure on the lung is higher when compared with healthy subjects due to the edema which increases lung weight causing an increase in pleural pressure gradient (i.e., this causes collapse of the dorsal dependent regions).
- **Cardiac mass** (the mass of the heart overlying both lungs): In ALI-ARDS patients, the cardiac mass is usually heavier compared to healthy subjects. This increases the pleural pressure gradient.
- **Cephalic displacement of the dorsal regions of the diaphragm:** In ALI-ARDS patients, this may be induced by sedation and paralysis, which in turn suppress the muscular tone of the diaphragm. This increases pleural pressure gradient.
- **Lung mass/shape:** In ALI-ARDS patients, it may increase pleural pressure gradient.

b- In the Prone Position:

- In ALI-ARDS patients, prone position increases regional lung inflation in the dorsal regions and decreases it in the ventral regions (by reducing the pleural pressure gradient). This occurs by the following:
  - In the prone position, there is an increase in the superimposed pressure on the lung in the ventral regions which collapse.
  - In the prone position, the cardiac mass lies on the sternum without acting as a compressive force on the lungs.
  - In the prone position, there is decreased abdominal pressure by unloading the weight of the abdominal content against the diaphragm. This leads to reduction of cephalic displacement of the diaphragm.
  - In the prone position, the change in the thoracic-lung shape decreases the pleural pressure gradient (figure 12-41).

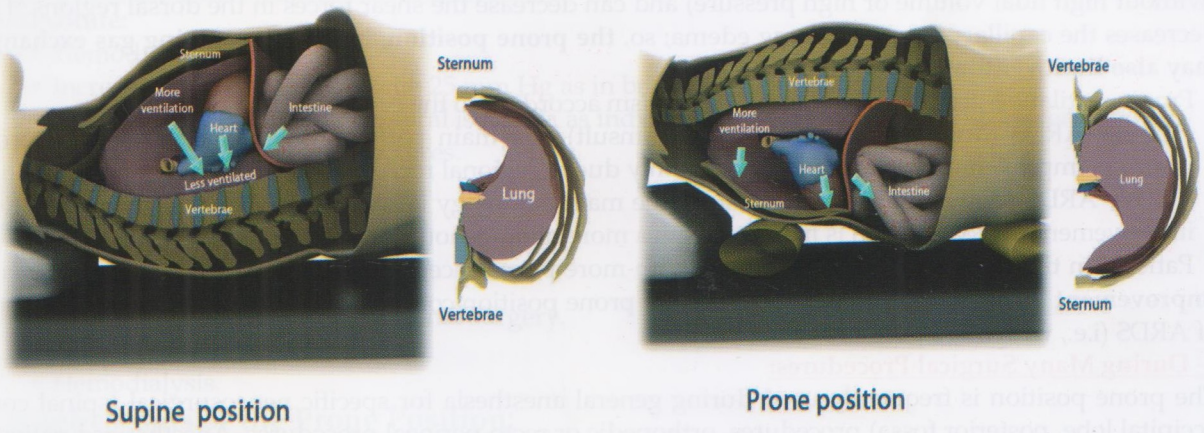


Figure 12-41: Effect of prone ventilation

IV) Alveolar Ventilation:

a- In the Supine Position: In ALI/ARDS, there is increased alveolar ventilation in the non-dependent ventral regions.

b- In the Prone Position: In ALI/ARDS, there is increased alveolar ventilation in the non-dependent dorsal regions causing more homogenous alveolar ventilatory distribution.

V) Pulmonary Perfusion:

a- In the Supine Position:

In healthy subjects, due to the effect of gravity, there is increased pulmonary perfusion in the dependent lung regions.

In ALI-ARDS patients, pulmonary perfusion is non-gravity dependent.

b- In the Prone Position:

In ALI-ARDS patients, there is more homogenous distribution of blood flow i.e., similar in dependent and non-dependent lung regions as it is not affected by gravity; therefore, it is not affected by changing the patient's position.

VI) Clearance of Secretions:

The prone position allows good secretion removal.

Clinical Uses of Prone Position

1- In acute Respiratory Failure (ALI-ARDS):

• Although prone position ventilation has been shown to be effective in improving arterial oxygenation, its **effects on patient outcome are still not clear;** so, it should not be adopted in all ALI-ARDS patients, but **limited to the most severe cases of respiratory failure**.

• The **exact time** of application of prone position ventilation **is not known,** but it is better to be applied **in the early phase of ALI-ARDS**.

• The **duration** of use of prone position ventilation **is not known**. Some authors continue to use prone position ventilation **until an arterial oxygenation of at least 13.3 KPa (100 mm Hg) is reached with a PEEP of 10 cm H_2O and an FiO_2 of 0.4**. Then they return to supine ventilation and begin an assisted mode of ventilation plus weaning procedures.

• The prone position can **increase the beneficial effect of PEEP** on improving arterial oxygenation and lower required PEEP levels to maintain this increase.

• **When nitric oxide (NO) is inhaled** by a patient in prone position ventilation, it causes a **greater improvement** in arterial oxygenation than any treatment used alone. It also decreases the required dose of NO, thus decreasing the accumulation of toxic pro-inflammatory degradation products such as nitrogen dioxide (NO_2).

• **Ventilation-induced lung injury** and the prone position:

The use of high trans-pulmonary pressures (i.e., ventilation with high tidal volume or high pressure) which overstretch the alveoli can cause epithelial and endothelial disruption and induce lung edema. Furthermore, failure to apply adequate PEEP levels can further increase the shear forces resulting from repeated air space opening and closure.

The prone position, by reducing the pleural pressure gradient, can increase trans-pulmonary pressure (without high tidal volume or high pressure) and can decrease the shear forces in the dorsal regions. This decreases the capillary stress and lung edema; so, **the prone position, besides improving gas exchange, may also limit ventilation-induced lung injury**.

• Prone ventilation produces a different mechanism according to the cause of ALI/ARDS:

- In 2ry ARDS (due to an extra-pulmonary insult), the main pathology is atelectasis. In the prone position, improvement of oxygenation is mainly due to regional recruitment due to lung mass/shape.
- In 1ry ARDS (due to a pulmonary insult), the main pathology is consolidation. In the prone position, improvement of oxygenation is mainly due to a more homogenous intra-tidal gas distribution.

• Patients in the **early phase of ARDS** (i.e., with more pronounced pulmonary edema) **exhibit a greater improvement** in arterial oxygenation during the prone position compared with patients in the late phase of ARDS (i.e., with more pulmonary fibrosis).

2- During Many Surgical Procedures:

The prone position is frequently used during general anesthesia for specific neurosurgical (spinal cord, occipital lobe, posterior fossa) procedures, orthopedic or recto-perineal procedures. Anesthetized patients, when breathing spontaneously in the prone position, are unable to maintain an adequate tidal volume and show a concomitant decrease in arterial oxygenation; therefore, mechanical ventilation should be applied in the prone position.

3- Prone Ventilation in Obese Patients:

• In obese patients, there is increased intra-abdominal pressure resulting in a more cranial shift of the diaphragm i.e., producing a marked decrease in lung volume and decreased movement of the dependent parts of the diaphragm. This causes more atelectasis and decreases oxygenation.

• The beneficial effects of the prone position may be greater in obese patients compared with normal subjects, due to a greater reduction in the intra-abdominal pressure and in the abdominal-to-diaphragmatic load. This causes a greater improvement in lung volume, oxygenation and respiratory mechanics.

Performance and Technique of the Prone Position:

• **Before starting** the turning sequence, an adequate level of **sedation or induction of anesthesia** during supine position (which may also require neuromuscular blockade) must be achieved to maximize patient compliance with the ventilation. An armored tube may be needed and securely taped to prevent dislodgement and loosening of the tape from drainage of saliva when prone.

• **Tracheal suctioning** is performed before turning, to prevent mobilization of airway secretions during the maneuver.

• All patients, during turning and once in the prone position, should be **monitored** with ECG, pulse oximetry and invasive arterial blood pressure. The monitors and breathing circuits may be discontinued briefly.

• At least 5 attendants (**one doctor and 4 nurses**) are required to perform the maneuver. The doctor usually places himself at the patient's head and is responsible for the endotracheal tube or tracheostomy tube and the breathing system connections. The four nurses, two on each side, turn the patient first to the lateral position, and sequentially to the prone position. The patient is turned as one unit with keeping the neck in line with the spine and arms of patients are placed beside him on turning the patient.

• **2 thick pillows** are put **under the shoulder** and **under the bony pelvis** respectively. This allows free abdominal wall motion and avoids inferior vena cava obstruction and tension-free positioning of the head. Sometimes, the thorax is generally supported by firm rolls or bolsters placed under the patient's sides from the clavicle to the iliac crest. Multiple commercial rolls/bolsters are available. All devices serve to relieve abdominal compression by the operating room table and maintain normal pulmonary compliance (to avoid pressure on the diaphragm cephalad, the inferior vena cava, and the aorta).

• **The arms can lie parallel** to the body or **with abducted shoulders < 90 degrees and flexed elbows** alongside the head while **the head turned** either to the right or left, avoiding extreme cervical rotation. Sometimes, the head is kept in a neutral position by using a surgical pillow, horseshoe headrest, or Mayfield pins. **The eyes should be protected** from pressure applied over them. Elastic stockings will be needed for the lower extremities to minimize pooling of blood especially with any flexion of the body.

• The **female breasts** should be placed freely (usually medial to the bolsters) and **male genitalia** should lie freely between thighs to prevent ischemic tissue injury.

• Monitors, i.v. lines, and breathing circuits must be reconnected as soon as possible.

Contraindications to the Prone Position:

a- Absolute:

- Hemodynamic instability.
- Increased intracranial tension > 25 mm Hg as in brain-injured patients.
- Patients with evidence of cerebral ischemia as indicated by a low jugular venous oxygen tension.
- Unstable spinal or pelvic fractures.

b- Relative:

- Face injury.
- Uncontrolled dysrhythmias.
- Acute bleeding.
- Recent tracheostomy or abdominal surgery.
- Broncho-pleural fistula.
- Hemodialysis.

Complications of the Prone Position:

a- Acute complications:

- **Compression on eyes** (causing retinal ischemia), nose (ischemic necrosis), knee, genitalia in males and breast in females (causing organ injuries).
- **Pressure sores.**
- **Nerve injury** such as:
  - Turning of the head position stretching the brachial plexus against anchors in the shoulder.
  - Closure of the retro-clavicular space by chest support with arms at the sides where the neurovascular bundle is trapped against the first rib.
  - The head of the humerus may thrust into neurovascular bundle if the arm and axilla are not relaxed.
  - Compression of the ulnar nerve in the cubital tunnel.
  - Compression of the radial nerve above the elbow.
- **Thoracic outlet obstruction:** it occurs if the arms is abducted at the shoulders to > 90 degrees. This can be preoperatively assessed if prone position is indicated by asking the patient preoperatively to elevate his arms abducted > 90 degrees (i.e., a surrender position). If coldness, pain, or tingling occurs, this suggests potential for thoracic outlet obstruction. Therefore, during prone positioning, it is better to let the arms tucked at the sides.
- Accidental displacement of the tracheostomy or endotracheal tube.

- Loss of venous access.
- Increased need for sedation and muscle relaxants.
- Increased need for immediate tracheal suctioning.
- Extreme head rotation that may decrease cerebral venous drainage (with facial edema) and decrease cerebral blood flow.
- Postural hypotension.
- Abdominal compression that may cause impairment of ventilation or inferior vena cava obstruction with venous congestion and increased blood loss.

b- Chronic complications in intensive care units:

- Contractures and calcifications of shoulder and hip joints.
- Nerve lesions.

Unilateral Decreased Breath Sounds during General Anesthesia

Causes:

1- Inadvertent placement or migration of an endotracheal tube into one bronchus especially the right. Trendelenburg (head down position) may advance the tip of the endotracheal tube 1-2 cm.
2- Pneumothorax.
3- Atelectasis.
4- Mucous plug.

Precautions:

1. The chest should be auscultated for equal breath sounds during:
   - Initial placement of the tube and its fixation.
   - Positioning of patients.
2. The tube position is confirmed by the length marks on tubes.
   - Adult male: 20-22 cm at teeth.
   - Adult female: 19-21 cm at teeth.
   - Children: Age/2 + 12.
3. The cuff of the tube should be felt in the supra-sternal notch.

Pulmonary Atelectasis and Collapse

It is collapse of a lobe, a segment of the lung (i.e., macroatelectasis) or even small number of alveoli (i.e., microatelectasis).

Causes:

a- Macroatelectasis:

- Bronchial obstruction (e.g., sputum retention, foreign body aspiration, blood clot, vomitus, misplaced endotracheal tube).
- Air space compression by heavy edematous lung tissue.
- External compression e.g., pleural effusion or hemothorax.
- Sputum retention may occur in the following cases:
  - Ciliary clearance is reduced (e.g., smoking or sedatives).
  - Mucus volume is excessive (e.g., asthma, bronchiectasis, cystic fibrosis, chronic bronchitis).
  - Inadequate coughing (e.g., COPD, pain, neuromuscular diseases).
  - Increased mucus viscosity (hypovolemia, inadequate humidification of inspired gas, cystic fibrosis).

b- Microatelectasis:

- Inadequate depth of respiration such as postoperatively after thoracic surgery.
- Nitrogen washout by 100% oxygen with subsequent absorption of O_2 occurring at a rate greater than replenishment i.e., absorption atelectasis.

Clinical Picture:

- Clinical picture of the cause may be apparent.
- Dyspnea and hypoxemia
- Circulatory collapse occurs if there is severe collapse.

Investigations:

1- Plain chest x-rays: show a collapsed lobe, segment or macroatelectasis.
2- If PA-aO_2 difference is high, it indicates microatelectasis.

3- Arterial blood gases show hypoxia.
4- Pulmonary compliance is reduced.
5- CT scan can be diagnostic.

Management:

a- Preventive Measures:

1- Sputum hydration:

- Maintenance of systemic hydration.
- Humidification of inspired gases e.g., nebulized saline/bronchodilators, heated water bath, or heat-moisture exchange filter.

2- Postoperative analgesia.

3- Physiotherapy:

- Postural drainage.
- Percussion and vibration.
- Manual hyperinflation.
- Intermittent positive pressure ventilation.
- Incentive spirometry.

4- Maintenance of lung volumes:

- Increased tidal volume.
- Continuous positive airway pressure ventilation (CPAP).
- Positive end expiratory pressure (PEEP).
- Positioning to reduce compression of lung tissue by edema.

b- Active Treatment:

- Specific management of the cause is important such as removal of foreign body or blood clot by bronchoscopy.
- All preventive measures should be continued.

Drowning and Near-Drowning

Definition: - Drowning is death from asphyxia during submersion in water.
- Near-drowning is used when the victim survives the initial insult.

Pathophysiology:

- Some victims suffer from **asphyxia** due to spastic closure of vocal cords to prevent water from entering into the trachea.
- **Aspiration of gastric contents** may occur when the patient loses consciousness.
- If the patient **inhales water**, three events may occur:
  - Marked **intrapulmonary shunting** producing marked ventilation/perfusion mismatching.
  - **Reflex bronchospasm.**
  - **Loss of pulmonary surfactant.**
- If the inhaled water is **fresh (hypotonic),** it is rapidly absorbed by the pulmonary circulation (> 800 mL is absorbed). This causes **hemodilution, hyponatremia, and even hemolysis.**
- If the inhaled water is **salt (hypertonic),** it draws out water from the pulmonary circulation. This causes **hemoconcentration, hypernatremia, hypermagnesemia, and hypercalcemia.**
- Drowning in **cold water** causes:
  - Loss of consciousness when body temperature becomes < 32 °C.
  - Ventricular fibrillation when body temperature becomes 28-29 °C.

Hypothermia has a protective effect on the brain which may improve survival.

Clinical Picture:

- Hypoxemia, hypercarbia and metabolic acidosis are common.
- Other injuries as spine fractures (after diving accidents) may occur.
- Neurological impairment is generally related to the duration of the submersion. Cerebral edema occurs after prolonged asphyxia.
- ARDS may occur after resuscitation.

Treatment:

1. Immediate correction of asphyxia by:
   - Clearing and establishing the airway.

- Administering O_2.

2. Cardio-pulmonary resuscitation should start when indicated.
   - In-line stabilization of the cervical spine during intubation is important.
   - Abdominal thrusts should be avoided because they may promote aspiration of gastric contents.
3. Gradual warming of the patient over a few hours is performed, if the patient is hypothermic.

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CARDIOVASCULAR DISEASES

13

- Physiological considerations
  - Cardiac action potentials
  - Innervation of the heart
  - Determinants of ventricular performance
  - Assessment of ventricular function
  - Cardiac cycle
  - Arterial blood pressure
  - Coronary circulation
  - Derived hemodynamic variables
- Prediction and risk assessment of a cardiac patient (risk stratification)
- Hypertension
- Ischemic heart disease
- Myocardial stunning and hibernation
- Valvular heart disease
- Mitral valve prolapse
- Pulmonary hypertension and Cor pulmonale
- Cardiomyopathy
- Heart failure (ventricular dysfunction)
- Shock
- Cardiac dysrhythmias
- Ventricular pre-excitation syndromes
- Prolonged QT interval syndrome
- Heart block
- Defibrillator
- Pacemaker
- Automatic implantable cardioverter defibrillator
- Integrated cardiopulmonary function capacity and cardiopulmonary exercise testing

Physiological Considerations

Cardiac Action Potentials

- The myocardial cell membrane is normally permeable to K^+, but relatively impermeable to Na^+. A membrane bound Na^+-K^+ ATPase concentrates K^+ intracellularly in exchange for Na^+ extrusion out of cells; therefore, intracellular Na^+ is kept low while intracellular K^+ is kept high relative to the extracellular space. Relative impermeability of the membrane to Ca^{++} also maintains a high extracellular to intracellular Ca^{++} gradient.
- An electrical potential is established across the cell membrane with the inside of the cell negative with respect to the extracellular space as anions remain inside the cells with their negative charges.
- The resting membrane potential represents the balance between 2 opposing forces:
  - The movement of K^+ down its concentration gradient out of the cell.
  - The electrical attraction of the negative charged intracellular space for the positive charged K^+ ions.

Phase	Name	Event (figure 13-1)	Cellular ion Movement	Remarks
0	Upstroke	Opening of fast Na^+ channels and decreased permeability to K^+.	Na^+ in	Peak up to +20 mV.
1	Early rapid repolarization	Closure of fast Na^+ channels and transient increase in permeability to K^+.	K^+ out	
2	Plateau	Opening of slow Ca^{++} channels.	Ca^{++} in	Last 0.2-0.3 sec
3	Final repolarization	Closure of slow Ca^{++} channels and increased permeability to K^+.	K^+ out	
4	Resting potential or diastolic repolarization	Normal permeability restored (atrial and ventricular cells) Intrinsic slow leakage of Na^+ and possible Ca^{++} entry into the cells that spontaneously depolarize	K^+ out & Na^+ (Ca^{++}??) in	Resting membrane potential -80 to - 90 mV (-50 to -60 mV in sino-atrial node)

Automaticity: It is the ability of self excitation and initiation of an impulse.

Excitability: It is measured by the strength of an electrical impulse required to excite the heart when applied at selected times in the cardiac cycle.

Innervation of the Heart

Sympathetic System	Parasympathetic System
• Via T_{1-4} by cervical (stellate) ganglia forming the cardiac plexus. • It supplies the atria, conducting tissues and ventricles. • β_1 adrenergic receptors stimulated by norepinephrine. • It causes: - positive chronotropic action (i.e., increased heart rate). - positive dromotropic action (i.e., increased atrio-ventricular conduction). and - positive inotropic action (i.e., increased contractility). N.B.: • There are few β_2 adrenergic receptors in the atria mainly, leading to positive chronotropic action. • There are also few α_1 adrenergic receptors, leading to minimal positive inotropic action.	• Via the vagus nerve. • It supplies the atria and conducting tissues only. • Muscarinic M_2 receptors stimulated by acetylcholine. • It causes: - negative chronotropic action. - negative dromotropic action. and - negative inotropic action. N.B.: • Increased vagal activity may stop spontaneous depolarization resulting in asystole until an impulse is generated by a pacemaker cell further down the system (i.e., vagal escape).

N.B.: The right sympathetic system and the right vagus nerve supply the sino-atrial (SA) node.
The left sympathetic system and the left vagus nerve supply the atrio-ventricular (AV) node.

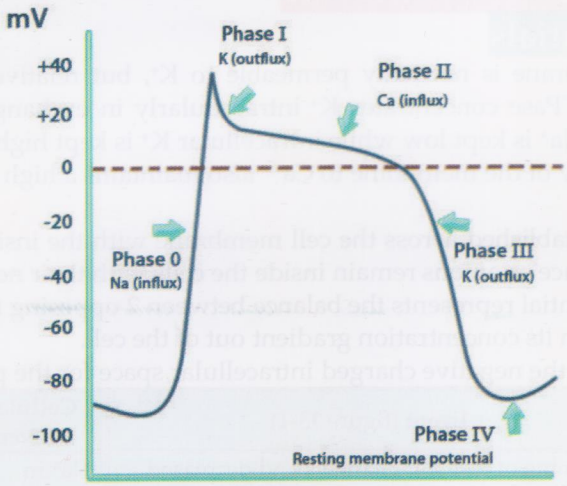


Figure 13-1: Action potential of ventricular muscle fibers

Determinants of Ventricular Performance

The ventricular function is either
- systolic function which involves ventricular ejection. It is most often related to cardiac output, or
- diastolic function which involves ventricular filling.

Cardiac Output (CO)

It is the volume of blood pumped by the heart per minute.
CO = Stroke volume x Heart rate
= 70 mL x 70 beat/min = 5 L/min in a 70 kg man normally.

Cardiac Index (CI)

$$CI = \frac{CO}{\text{Body surface area}} = 3\ L/min/m^2$$ in a 70 kg man (range 2.5-4.2 L/min/m^2)

Body surface area is usually obtained from nomogram based on height and weight of the individual (figure 13-2).

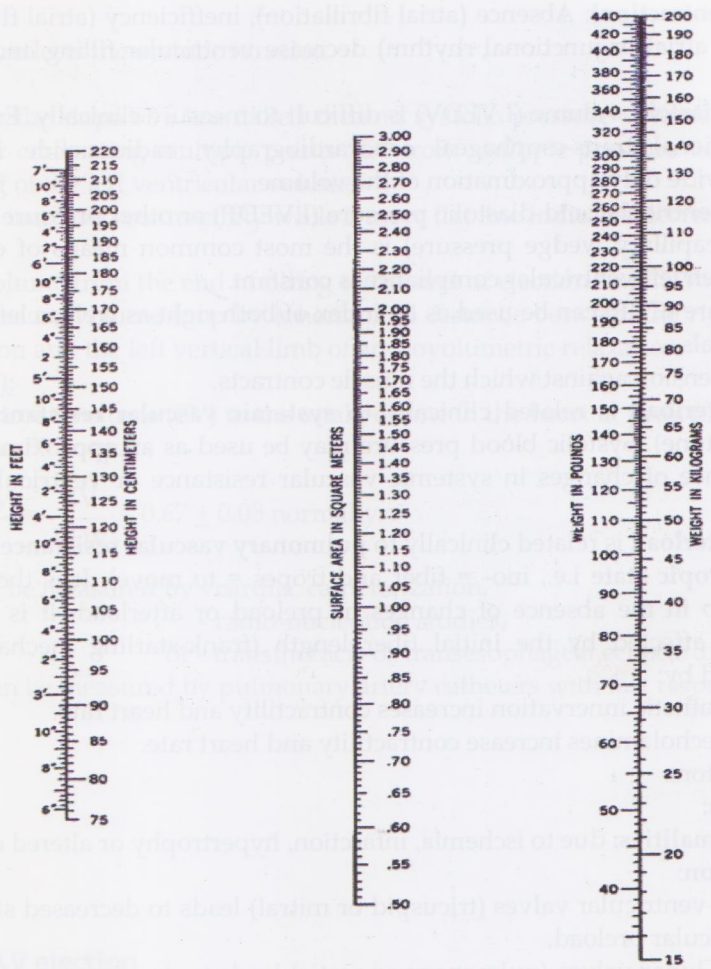


Figure 13-2: Nomograms for calculating body surface area of adults

Control of Cardiac Output:

I. Heart Rate:

Increased heart rate is accompanied by an increase in contractility (Bowditch effect or Staircase phenomenon). The normal intrinsic rate of SA node in young adults is about 90-100 beats/min, but it decreases with age based on the following formula:

Normal intrinsic heart rate = 118 beats/min – (0.57 x age)

II. Stroke Volume:

It is the volume pumped per contraction.

Factors affecting the stroke volume:

1- Preload: It is muscle length prior to contractions. It represents the end-diastolic volume and depends on ventricular filling.

Factors affecting ventricular filling (preload):

- **Venous return**: It is the most important factor.
- **Blood volume**: It is important perioperatively.
- **Distribution of blood volume**: It is affected by:

- Posture.
- Intrathoracic pressure e.g., during positive pressure ventilation or thoracotomy.
- Pericardial pressure e.g., pericardial diseases.
- Venous tone: While other factors are relatively fixed, venous tone is easily variable.

- **Heart rate**: Increased heart rate is associated with proportionately greater reductions in diastole than systole; therefore, ventricular filling progressively becomes impaired at high heart rate (> 120 beats/min in adults).

• **Rhythm (atrial contraction)**: Absence (atrial fibrillation), inefficiency (atrial flutter), or altered timing of contraction (low atrial or junctional rhythm) decrease ventricular filling and cardiac output by 20-30%.

Left ventricular end-diastolic volume (LVEDV) is difficult to measure clinically. Even imaging techniques such as two-dimensional trans-esophageal echocardiography, radionuclide imaging, and contrast ventriculography provide only approximation of the volume.

Measurement of left ventricular end-diastolic pressure (LVEDP) or other pressure approximating LVEDP (such as pulmonary capillary wedge pressure) is the most common means of estimating LVEDV and preload especially when left ventricular compliance is constant.

Central venous pressure (CVP) can be used as an index of both right as well as left ventricular preload in most normal individuals.

2- Afterload: It is the tension against which the muscle contracts.

• **Left** ventricular **afterload** is related clinically to **systemic vascular resistance** (the latter is mainly affected by arteriolar tone). Systolic blood pressure may be used as an approximation of left ventricular afterload in the absence of changes in systemic vascular resistance or ventricular wall size, shape, or thickness.

• **Right** ventricular **afterload** is related clinically to **pulmonary vascular resistance**

3- Contractility (inotropic state i.e., ino- = fiber and tropes = to move): It is the intrinsic ability of the myocardium to pump in the absence of changes in preload or afterload. It is related to the force of contraction which is affected by the initial fiber length (frank-starling mechanism) (Starling's law). Contractility is affected by:

• Neural factor: Sympathetic innervation increases contractility and heart rate.
• Humoral factor: Catecholamines increase contractility and heart rate.
• Pharmacological factors.

4- Geometrical factors:

a- Wall motion abnormalities: due to ischemia, infarction, hypertrophy or altered conduction.

b- Valvular dysfunction:

• Stenosis of the atrio-ventricular valves (tricuspid or mitral) leads to decreased stroke volume primarily by a decrease in ventricular preload.
• Stenosis of the semi-lunar valves (pulmonary or aortic) leads to decreased stroke volume primarily by an increase in ventricular afterload.
• Regurgitation of atrio-ventricular valves leads to a fraction of the stroke volume returning backward into the atrium during systole.
• Regurgitation of the semi-lunar valves leading to a fraction of the stroke volume returning backward into the ventricle during diastole.

Assessment of Ventricular Function

1- Tissue perfusion assessment.
2- Central venous pressure assessment.
3- Pulmonary artery catheter (for measuring the derived hemodynamics).
4- Cardiac output measurement.
5- Trans-thoracic or trans-esophageal echocardiography.

All these measurements are discussed in full details in the chapter of "Monitoring during Anesthesia and Intensive Care".

6- Pressure Volume Loops (PV Loops):

They show the relationship between the left ventricular volume and left ventricular pressure during a single cardiac cycle. It is best obtained by combination of trans-esophageal echocardiography and pulmonary artery catheterization (figure 13-3).

The normal pressure-volume loop shows:

• **Left Ventricular Compliance:**

It is the relationship between the change in pressure and change in volume of the left ventricle and is defined as the slope of the filling phase or segment "AB", where an increased slope means decreased compliance and vice versa.

• **End-Diastolic Point:**

It is the point B" and reflects the diastolic function.

• **End-Systolic Point:**
It is the point "D" and reflects the systolic function.
• **Contractility:**
It may be illustrated by the slope of a line called the end systolic pressure-volume relationship (ESPVR). This slope is created by connecting multiple points "D" from multiple pressure-volume loops generated by changes in the filling of the left ventricular volume.
A steeper line indicates increased contractility while a more flat line indicates decreased contractility.
• **Stroke Volume (SV):**
It is the difference in volume from the end of filling to the end of ejection i.e., EDV – ESV; therefore, it can be shown from the pressure-volume loop by a horizontal distance between the right vertical limb of an isovolumetric contraction and the left vertical limb of an isovolumetric relaxation.

• **Ejection Fraction (EF):**
It is the ratio between stroke volume (SV) to the total volume in the heart at peak filling i.e., SV/ EDV; so, it can be shown from the PV loop.

$$EF = \frac{EDV \quad ESV}{EDV} = \frac{SV}{EDV} = 0.67 \pm 0.08 \text{ normally.}$$

Left ventricular EF: can be measured by - cardiac catheterization,
- radio-nucleotide studies,
or - transthoracic or transesophageal echocardiography.
Right ventricular EF: can be measured by pulmonary artery catheters with fast response thermistors.

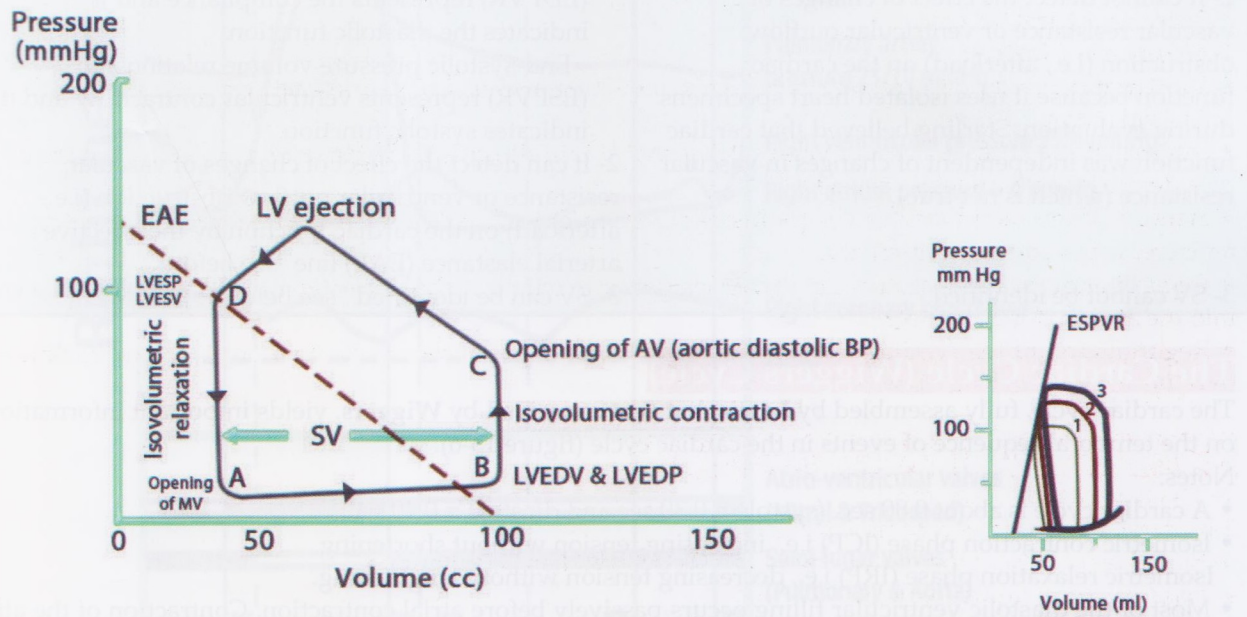
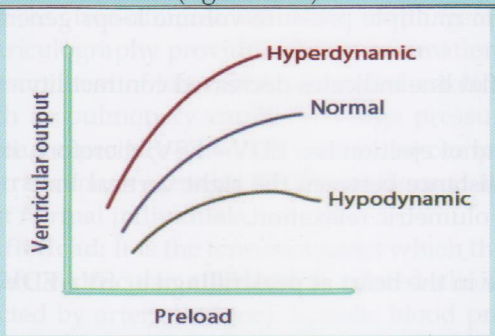
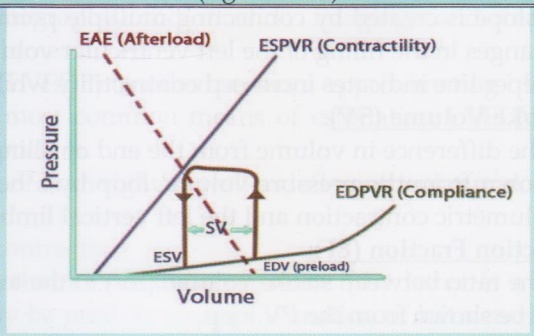


Figure 13-3: A normal PV loop (left) and the effect of changes of the preload on contractility (right)

A = Opening of the mitral valve (MV), left ventricular end systolic volume (LVESV) and early diastolic pressure.
B = Closure of the MV, Left ventricular end diastolic pressure and volume (LVEDP and LVEDV).
C = Opening of the aortic valve (AV) and systemic aortic diastolic pressure.
D = Closure of the AV, left ventricular end systolic pressure (LVESP), LVESV and it coincides with the dicrotic notch in aortic pressure tracing.
• **Effective Arterial Elastance (EAE):**
It is the line drawn from a point on the X-axis correlated to end-diastolic volume through the upper left shoulder of the loop i.e., D point. Change in the slope of EAE line shows the effects of peripheral vascular resistance. If the EAE line is shifted to the left, this indicates vasodilatation while if the EAE line is shifted to the right, this indicates vasoconstriction.

Difference between Starling Curves of Ventricular Function and Pressure-Volume Loops of the Left Ventricle:

Starling Curves of Ventricular Function (figure 13-4)	Pressure-Volume Loops of Left Ventricle (figure 13-5)
 Figure 13-4	 Figure 13-5
• It was obtained by Ernest Starling around 1900.	• It is best obtained by combination of trans-esophageal echocardiography and pulmonary artery catheterization.
• It is less valuable.	• It is more valuable.
• Disadvantages:	• Advantages:
1- It **cannot detect the effect of compliance** as it uses RA pressure to represent the preload.	1- It **can detect the effect of compliance** as: ▫ End-diastolic pressure volume relationship (EDPVR) represents the compliance and it indicates the diastolic function. ▫ End-systolic pressure volume relationship (ESPVR) represents ventricular contractility and it indicates systolic function.
2- It cannot detect the effect of changes of vascular resistance or ventricular outflow obstruction (i.e., afterload) on the cardiac function because it uses isolated heart specimens during evaluation. Starling believed that cardiac function was independent of changes in vascular resistance (which is not true).	2- It can detect the effect of changes of vascular resistance or ventricular outflow obstruction (i.e., afterload) on the cardiac function by the effective arterial elastance (EAE) line "see before".
3- SV cannot be identified.	3- SV can be identified "see before".

The Cardiac Cycle (Wiggers Cycle)

The cardiac cycle, fully assembled by **Lewis**, but first conceived by **Wiggers**, yields important information on the temporal sequence of events in the cardiac cycle (figure 13-6).

Notes:

- A cardiac cycle is about 0.80 sec. (systole = 0.30 sec and diastole = 0.40 sec).
- Isometric contraction phase (ICP) i.e., increasing tension without shortening.
  Isometric relaxation phase (IRP) i.e., decreasing tension without lengthening.
- Most of the diastolic ventricular filling occurs passively before atrial contraction. Contraction of the atria (atrial kick) normally contributes 20-30% of ventricular filling.
- The notch in the aortic pressure (incisura) is due to transient backflow of blood into the left ventricle just before aortic valve closure.
- Left coronary blood flow occurs mainly during diastole due to the large force of the left ventricular contraction which almost completely occludes the intra-myocardial part of the coronary arteries; in fact, blood flow may transiently reverse in epicardial vessels. Right coronary blood flow occurs during all the cardiac cycle (systole and diastole); therefore, diastolic blood pressure is the pressure which affects the left coronary perfusion pressure, while the mean blood pressure is the one that affects the right coronary perfusion pressure.

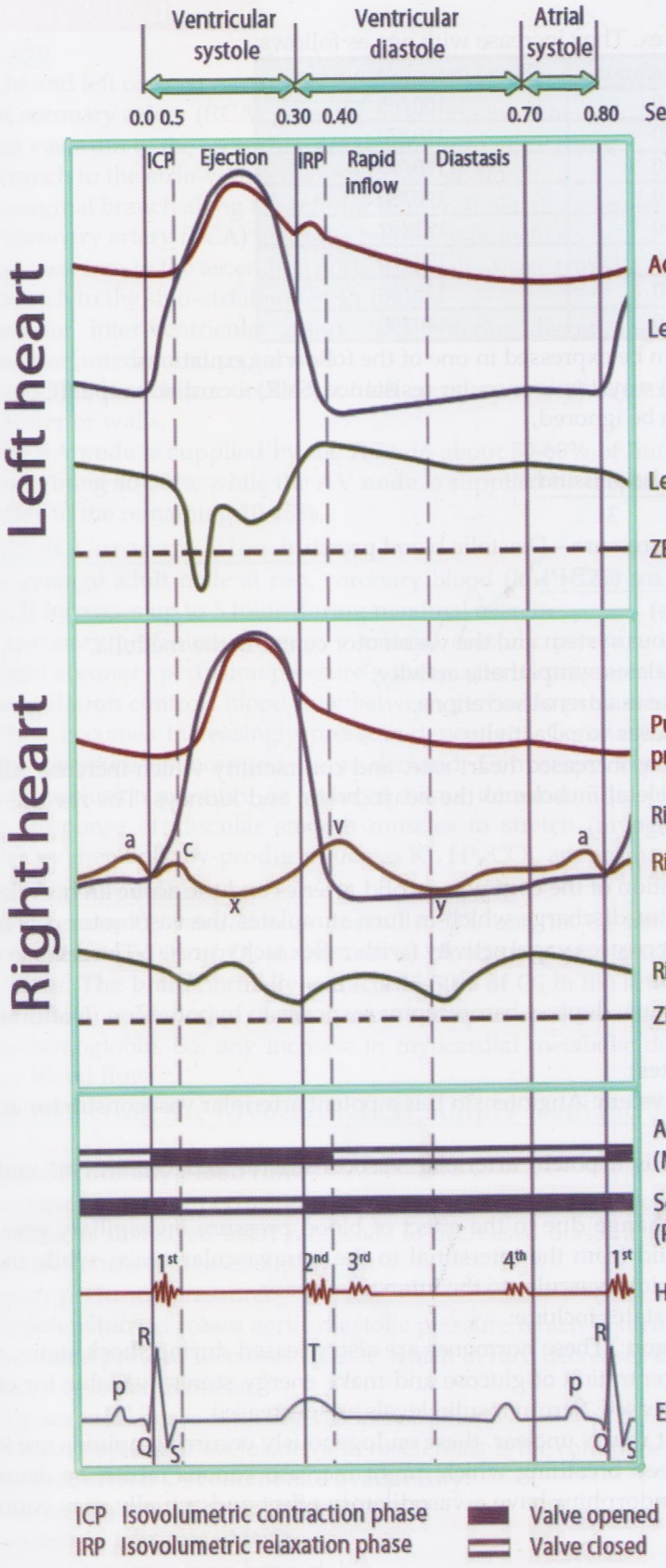


Figure 13-6: Cardiac cycle

Arterial Blood Pressure

The normal values vary with age and sex. They increase with age as follows:

Age (years)	Blood Pressure (mm Hg)
10	100/65
20	110/70
30	115/75
40	120/80
50	125/82
60	130/85
70	135/88
80	140/90

Mean arterial blood pressure (MAP) can be expressed in one of the following equations:

- MAP– central venous pressure (CVP) = systemic vascular resistance (SVR) x cardiac output (CO)

As CVP is normally very small and can be ignored,

MAP = SVR x CO

- MAP = Diastolic blood pressure + $\frac{\text{Pulse pressure}}{3}$

Where pulse pressure = Systolic blood pressure – Diastolic blood pressure

Control of Arterial Blood Pressure (ABP)

A) Immediate Control (within seconds)

It is the function of the autonomic nervous system and the vasomotor center in the medulla.

Decreased arterial blood pressure stimulates sympathetic activity,
increases adrenal secretions,
and decreases vagal activity.

This results in systemic vasoconstriction, increased heart rate, and contractility which increase ABP and distribute blood from the skin, gut, skeletal muscles to the heart, brain, and kidneys. The reverse occurs with increased ABP.

N.B.: **Baroreceptor Reflex**:

Baroreceptors are present in the bifurcation of the common carotid arteries and the aortic arch. A decrease in blood pressure decreases baroreceptor discharge which in turn stimulates the vasomotor center. This causes systemic vasoconstriction and decreases vagal activity (with reflex tachycardia). The reverse occurs with increased ABP.

All volatile anesthetics especially halothane depress baroreceptor response to hypotension (isoflurane and desflurane have the least effect).

B) Intermediate Control (within minutes)

By: • **Renin-angiotensin-aldosterone system**: Angiotensin II is a potent arteriolar vasoconstrictor and causes Na^+ and water retention.

• **Arginine vasopressin (AVP)**: It is a potent arteriolar vasoconstrictor and causes Na^+ and water retention.

• **Alteration in capillary fluid exchange** due to the effect of blood pressure on capillary pressure as decreased blood pressure shifts fluid from the interstitial to the intravascular space, while increased blood pressure shifts fluid from the intravascular to the interstitial space.

Other hormones released during shock states include:

• **Epinephrine, cortisol, and glucagon**: These hormones are also released during shock states, where they increase the extracellular concentration of glucose and make energy stores available for cellular metabolism. Fat mobilization is increased. Serum insulin levels are decreased.

• **Endorphins**: Although their exact role is unclear, these endogenously occurring opioids are known to decrease pain. They promote deep breathing which might increase venous return by decreasing intrathoracic vascular resistance. Endorphins have a vasodilatory effect and actually may counteract the sympathetic influence.

C) Long term Control (within hours)

By the kidney as decreased blood pressure leads to Na^+ (and H_2O) retention, while increased blood pressure leads to Na^+ (and H_2O) excretion.

Coronary Circulation

Anatomy:

The right and left coronary arteries arise from ostia in the right and left sinuses of the Valsalva.

a- Right coronary artery (RCA) gives the following branches:

- Vasa vasorum to the ascending aorta and pulmonary trunk.
- A branch to the atrio-ventricular node (AV node).
- A marginal branch along the inferior border. It usually supplies the left ventricular inferior wall.

b- Left coronary artery (LCA) gives the following branches:

- Vasa vasorum to the ascending aorta and pulmonary trunk.
- A branch to the sino-atrial node (SA node).
- Anterior inter-ventricular artery (left anterior descending artery). It usually supplies the left ventricular anterior and septal wall.
- Circumflex branch (continuation of left coronary artery). It usually supplies the left ventricular lateral and posterior walls.

N.B.: The **SA node** is supplied by the **RCA** in about **50-60%** of humans and by the **left circumflex** artery in the remaining **40-50%**, while the **AV node** is supplied by the **RCA** in **85-90%** of humans and by the **left circumflex** in the remaining **10-15%**.

Control of Coronary Blood Flow:

- In an average adult male at rest, coronary blood flow = 250 mL/min (70-100 mL/min/100 g of heart tissues). It increases up to 5 folds during maximal exercise.
- **Left** coronary perfusion pressure = **arterial** diastolic pressure - left ventricular end-diastolic pressure, while **right** coronary perfusion pressure = **mean** arterial pressure - right ventricular end-diastolic pressure.
- **Autoregulation** controls blood flow between perfusion pressures of **50-120 mm Hg**. Beyond this range, blood flow becomes increasingly pressure-dependent. Coronary arteries dilate in response to reduced perfusion pressure or increased tissue demand. Conversely, coronary arteries constrict in response to increased perfusion pressure or reduced tissue demand. This phenomenon is likely due to both the intrinsic response of vascular smooth muscles to stretch (myogenic theory) and the accumulation of vasodilatory metabolic by-products such as K^+, H^+, CO_2, adenosine, and lactate (metabolic theory).

Myocardial O_2 Balance

Coronary venous O_2 saturation is normally 30% and its O_2 tension is 30 mm Hg. **The myocardium** normally **extracts 65 % of O_2** in the arterial blood (it is near the maximum), compared to 25% in most other tissues. **The brain** normally **extracts 45-50% of O_2** in the arterial blood. Therefore, the myocardium (and the brain), unlike other tissues, cannot compensate for reductions in blood flow by extracting more O_2 from hemoglobin. So, any increase in myocardial metabolic demand must be met by an increase in coronary blood flow.

Factors Affecting the Myocardial O_2 Supply Demand Balance

A) Decreased O_2 Supply:

1. Decreased coronary blood flow

(i.e., decreased coronary perfusion pressure which equals diastolic blood pressure – LVEDP).

- Heart rate: as **increased heart rate** leads to decreased diastolic time (more than the decrease in systolic time) which in turn decreases supply.
- Coronary perfusion pressure:
  - **Hypotension** decreases aortic diastolic pressure which in turn decreases supply.
  - **Increased preload** increases LVEDP which in turn decreases supply.
- Coronary vascular diameter:
  - **Hypocapnia** causes coronary vasoconstriction.
  - Coronary spasm or occlusion (**atherosclerosis** is the commonest cause).

2. Decreased arterial O_2 content and availability:

- Anemia i.e., decreased hemoglobin.
- Hypoxemia i.e., decreased PaO_2.
- Decreased O_2 release from hemoglobin.

B) Increased O_2 Demand:

1. Heart rate: as **increased heart rate** leads to increased demand.

The maximum aerobic limit of heart rate = 230 - The patient's age in years, more than this heart rate, anerobic metabolism occurs resulting in ischemia.

2. **Increased basal requirement.**
3. Increased wall tension:
   - Increased preload (i.e., LVEDP) which in turn increases demand.
   - Increased afterload which in turn increases demand.
4. Increased contractility.

Derived Hemodynamic Variables

The derived hemodynamics are usually obtained by pulmonary artery catheters. They include: cardiac output, cardiac index, stroke volume, stroke volume index, left ventricular stroke work index, right ventricular stroke work index, systemic vascular resistance and its index, and pulmonary vascular resistance and its index. They are discussed in more details in the chapter of "Monitoring during Anesthesia & Intensive Care".

Other variables include:

- **Ejection Fraction (EF)** that is discussed above.
- **Diastolic-Pressure Time Index (DPTI)** = Coronary perfusion pressure x diastolic time

It is used as a measure of left ventricular blood flow **(O_2 Supply).**

- **Tension-Time Index (TTI)** = systolic blood pressure x systolic time.

It is used as a measure of **O_2 demand.**

- **Endocardial Viability Ratio:** It is the ratio of 2 indices DPTI / TTI = more than 1 normally.

It is used as a measure of **O_2 supply-demand balance.**

If it is < 0.7, it indicates subendocardial ischemia.

- **Rate-Pressure Product (RPP) or double product** = systolic arterial pressure x heart rate = 9600 mm Hg /min.
- **Triple Index (TI)** = systolic arterial pressure x heart rate x pulmonary capillary wedge pressure.

N.B.:

TTI, RPP, and TI measure myocardial **O_2 demand.**

Angina threshold for RPP ranges from 15 000-20 000 mm Hg/min.

It is usually recommended to keep RPP below 12 000 and TI below 150 000

High RPP and TI indicate a potential danger of ischemia, but normal or low values do not rule out ischemia. Patients with tachycardia and hypotension may have a normal RPP while both tachycardia and hypotension may produce ischemia.

Cardiovascular Pressures:

Pressure	Range (mm Hg)	Mean (mm Hg)
Central Venous Pressure (CVP)	0-8	4
Right atrial pressure	0-8	4
Right ventricular - systolic pressure	14-30	25
- end diastolic pressure	0-8	4
Pulmonary Artery - systolic pressure	15-30	25
- diastolic pressure	5-15	10
- mean	10-20	15
Pulmonary capillary wedge pressure (mean)	5-15	10
Left atrial pressure	4-12	7
Left ventricular - systolic pressure	90-140	120
- end diastolic pressure	4-12	7

In addition to the values of systemic blood pressure (discussed above).

Prediction and Risk Assessment of a Cardiac Patient (Risk Stratification)

Risk stratification consists of preoperative history and physical examination followed by a series of tests to predict perioperative cardiac morbidity and mortality.

Cardiovascular complications account for 25-50% of deaths after non-cardiac surgery; therefore, many trials have been done to predict the incidence and percentage of unwanted outcomes.

I) Goldman's Cardiac Risk Index in Non-Cardiac Surgery

It is postulated by Goldman et al., **1977**. It is used for non-cardiac surgery. Detsky modification of the Goldman cardiac risk index is postulated later on and is specific for vascular surgery:
With each system, a higher total score indicates increased risk of severe or significant cardiac complications.

Preoperative Risk Factors	Goldman Points	Detsky Points
History and examination		
• Age > 70 year old	5	5
• Myocardial infarction - less than 6 months	10	10
- more than 6 months	0	5
• Angina (Canadian Heart Association Classification):- class 3	Not available	10
- class 4	Not available	20
• Unstable angina within 3 months	Not available	10
• Alveolar pulmonary edema: < 1 week	Not available	10
> 1 week	Not available	5
• Signs of congestive heart failure (S_3 heart sound gallop or increased jugular venous pressure "distension").	11	Not available
• Aortic stenosis (significant or critical)	3	20
Investigations:		
• 12- lead ECG		
- Arrhythmia other than sinus or premature atrial beats	7	5
- Five or more premature ventricular ectopics per minute	7	5
• Poor general physical status as defined by any one of the following:	3	5
Arterial blood gases - PaO_2 < 60 mm Hg		
- $PaCO_2$ > 50 mm Hg		
- s. HCO_3^- < 20 mmol/L		
- s. K^+ < 3.0 mmol/L		
Renal function tests - s. urea > 7.5 mmol/L or > 50 mg/dL		
- s. creatinine > 270 µmol/L or > 3.0 mg/dL		
Liver function tests - s. aspartate amino-transferase (AST) i.e., s. glutamic-oxaloacetic transaminase (SGOT) abnormal		
- Chronic liver disease.		
Specific Type of surgery		
• Emergency Surgery	4	10
• Intra-peritoneal or intrathoracic	3	Not available
• Aortic surgery	3	Not available

The risk of major postoperative cardiac complications increases with increasing the points.

Class	Points		Incidence of Risk in Goldman	`Incidence of Risk in Detsky
	Goldman	Detsky		
I	0-5	0-15	0.3-3%	Low risk
II	6-12	20-30	1-10%	Intermediate risk
II	13-25	> 30	3-30%	High risk
IV (in Goldman only)	26-53	Not available	19-75%	Not available

II) In 1992, the Perioperative Ischemia Research Group Led by Hollenberg and Mangano Identified 5 Preoperative Predictors

1. Left ventricular hypertrophy by ECG.
2. History of hypertension.
3. History of diabetes mellitus.
4. Definite coronary artery disease.
5. Digoxin use

The risk of postoperative myocardial ischemia increased progressively with the numbers of predictors present.

III) In 1999, Lee et al, Identified 6 Preoperative Predictors (Revised Cardiac Risk Index)

It was used for patients undergoing elective major non-cardiac surgery.

1. High risk type of surgery (such as abdominal aortic aneurysm, peripheral vascular surgeries, thoracotomy, or major abdominal surgery).
2. History of ischemic heart disease.
3. History of congestive heart failure.
4. History of cerebro-vascular disease.
5. Insulin dependent diabetes mellitus.
6. Preoperative s. creatinine > 2.0 mg/dL (> 177 µmol/L).

The rate of major cardiac complications (such as myocardial infarction, pulmonary edema, ventricular fibrillation and primary cardiac arrest) was:
- If there are no predictors, 0.4-0.5%.
- If there is one predictor, 0.9-1.3%.
- If there are 2 predictors, 4-7%.
- If there are ≥ 3 predictors, 9-11%.

IV) Recently, the American College of Cardiology / American Heart Association (ACC/AHA) made the following guidelines and risk stratification strategy

Aim:
- For determining the need for preoperative cardiac evaluation.
- For identifying patients at increased risk so as to manage them and to lessen the risk and severity of perioperative cardiac events before non-cardiac surgery.

Guidelines are a Multi-Step Algorithm:

Step I: It assesses the urgency of surgery. The need for emergency surgery takes precedence over the need for additional work-up. It is discussed in figure 13-7.

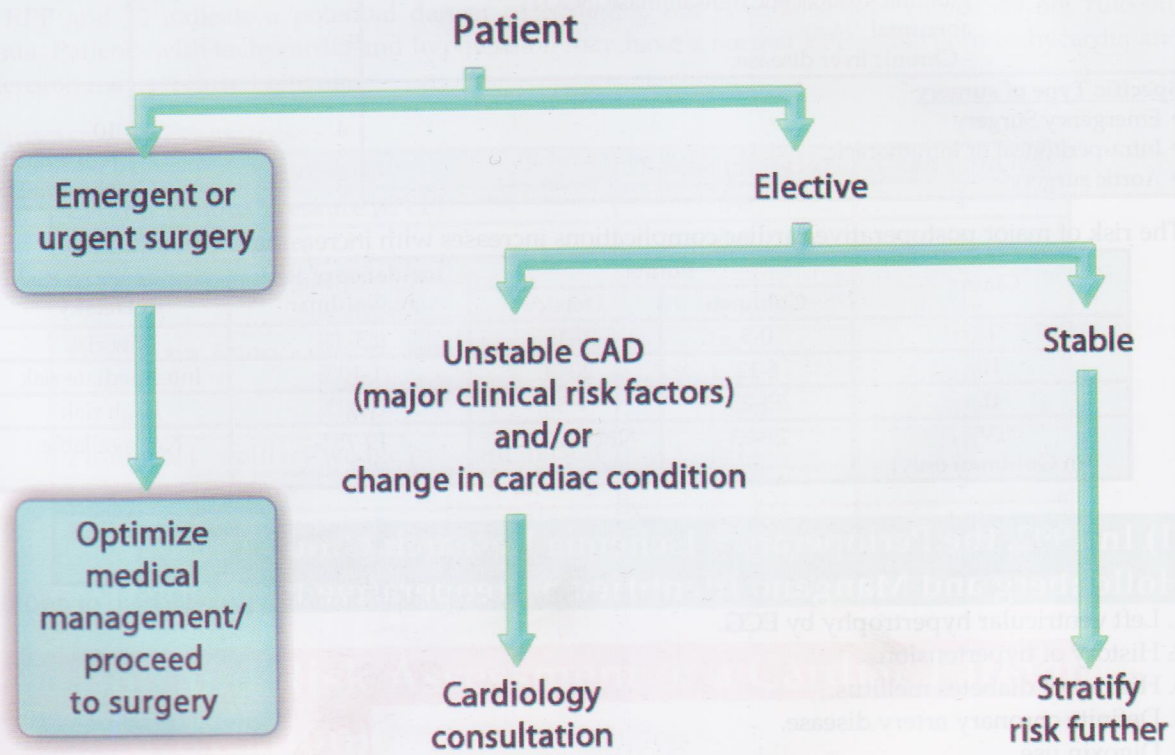


Figure 13-7: Assessment of the urgency of surgery

Step II: It assesses whether the patient has undergone revascularization. It is discussed in figure 13-8.

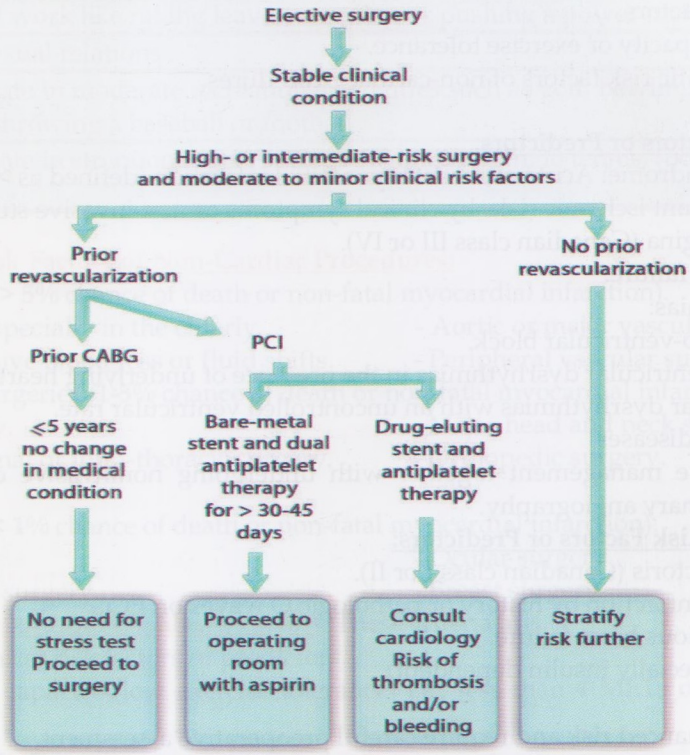


Figure 13-8: Assessment of prior revascularization

Step III: It determines whether and when the patient underwent invasive or noninvasive cardiac evaluation. It is discussed in figure 13-9.

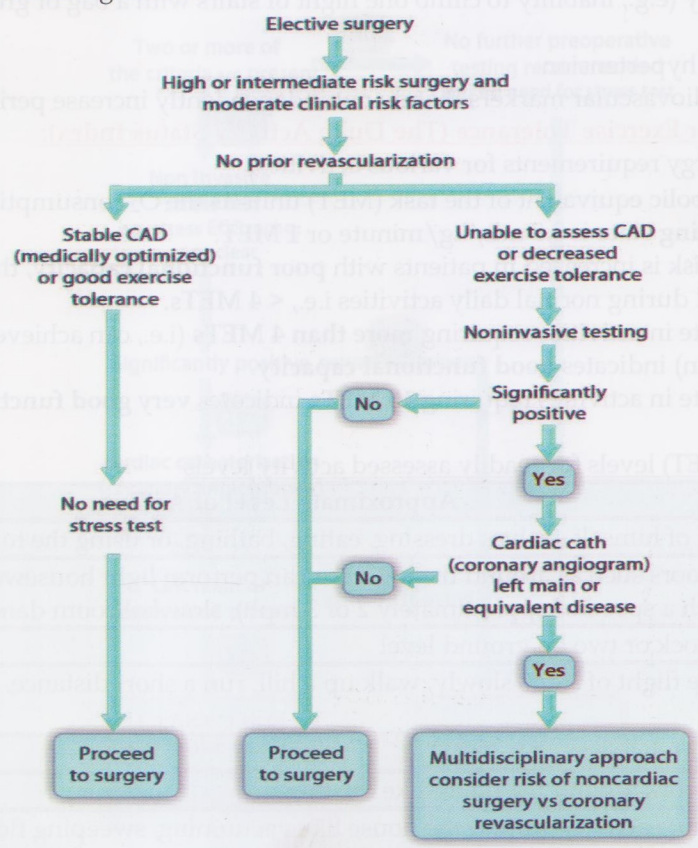


Figure 13-9: Assessment of the invasive or noninvasive cardiac evaluation

The Next Steps of the ACC/AHA guidelines integrate risk stratification according to the following 3 factors: 1- Clinical risk factors.
2- Functional capacity or exercise tolerance.
3- Surgery-specific risk factors of non-cardiac procedures.

1- Clinical Risk Factors:

Major Clinical Risk Factors or Predictors:

- Unstable coronary syndrome: Acute or recent myocardial infarction (defined as > 7 days, but ≤ 1 month) with evidence of important ischemic risks by clinical symptoms or non-invasive studies.
- Unstable or severe angina (Canadian class III or IV).
- Decompensated heart failure.
- Significant dysrhythmias:
  - High grade atrio-ventricular block.
  - Symptomatic ventricular dysrhythmias in the presence of underlying heart disease.
  - Supra-ventricular dysrhythmias with an uncontrolled ventricular rate.
- Severe valvular heart diseases.

They mandate intensive management together with undergoing noninvasive cardiac evaluation and when appropriate, coronary angiography.

Intermediate Clinical Risk Factors or Predictors:

- Mild stable angina pectoris (Canadian class I or II).
- Previous myocardial infarction by history or pathologic Q waves on ECG.
- Compensated or previous heart failure.
- Diabetes mellitus (especially insulin dependent).
- Renal insufficiency.

They are markers of enhanced risk and require careful preoperative assessment.

Minor Clinical Risk Factors or Predictors:

- Advanced age (> 70 years).
- Abnormal ECG (left ventricular hypertrophy, left bundle branch block, or ST-T abnormalities).
- Rhythm other than the sinus rhythm.
- Low functional capacity (e.g., inability to climb one flight of stairs with a bag of groceries).
- History of stroke.
- Uncontrolled systemic hypertension.

They are recognized cardiovascular markers that do not independently increase perioperative risk.

2- Functional Capacity or Exercise Tolerance (The Duke Activity Status Index):

- It is an estimate of energy requirements for various activities.
- It is expressed in **m**etabolic **e**quivalent of the **t**ask (MET) units as the O_2 consumption ($\dot{V}O_2$) of a 70 kg, 40 year-old man in a **resting state** is 3.5 mL/kg/minute or **1 MET**.
- Perioperative cardiac risk is increased in patients with **poor functional capacity**, that is, who are unable to meet a 4 MET demand during normal daily activities i.e., **< 4 METs**.
- The ability to participate in activities requiring **more than 4 METs** (i.e., can achieve O_2 consumption more than 14 mL/kg/min) indicates **good functional capacity**.
- The ability to participate in activities requiring **10 METs** indicates **very good functional capacity and very low risk**.

Metabolic equivalent (MET) levels for readily assessed activity levels

MET Score	Approximate Level of Activity
1	Take care of himself such as dressing, eating, bathing, or using the toilet
2	Walk indoors such as around the house or can perform light housework, baking, slow walk (with a speed of approximately 2 or 3 mph), slow ballroom dancing, Golf with a cart
3	Walk a block or two on ground level
4	Climb one flight of stairs slowly, walk up a hill, run a short distance, or lightly work at home
5	Run a short distance
6	Do light work around the house like dusting
7	Do moderate activity around the house like vacuuming, sweeping floors or carrying up groceries

8	Do heavy work around the house like scrubbing floors or moving heavy furniture
9	Do yard work like raking leaves, weeding or pushing a power mower
10	Have sexual relations
11	Participate in moderate recreational activities such as golf, bowling, dancing, double tennis, throwing a baseball or football
12	Participate in strenuous sport such as swimming, single tennis, football, basketball, or skiing

3- Surgery-Specific Risk Factors of Non-Cardiac Procedures:

a. High risk surgeries (**> 5%** chance of death or non-fatal myocardial infarction).
- Emergency surgery especially in the elderly.
- Procedures with massive blood loss or fluid shifts.
- Aortic or major vascular surgery.
- Peripheral vascular surgery.

b. Intermediate risk surgeries (**1-5%** chance of death or non-fatal myocardial infarction).
- Carotid artery surgery.
- Elective intra-abdominal or intra-thoracic surgery.
- Prostatic surgery.
- Major head and neck surgery.
- Orthopedic surgery.

c. Low risk surgeries (**< 1%** chance of death or non-fatal myocardial infarction).
- Endoscopic surgery.
- Peripheral superficial surgery.
- Ocular surgery.
- Breast surgery.

Three Criteria are Chosen from the above Factors. These criteria are:

1- Intermediate clinical risk factors or predictors.

2- Poor functional capacity (low exercise tolerance) i.e., less than 4 METs or inability to determine exercise tolerance.

3- High risk surgery.

Patients who have **2 or more of the above criteria** could be considered **for further cardiac evaluation**.

The Next Steps determine the need for invasive or noninvasive cardiac tests as shown in figure 13-10

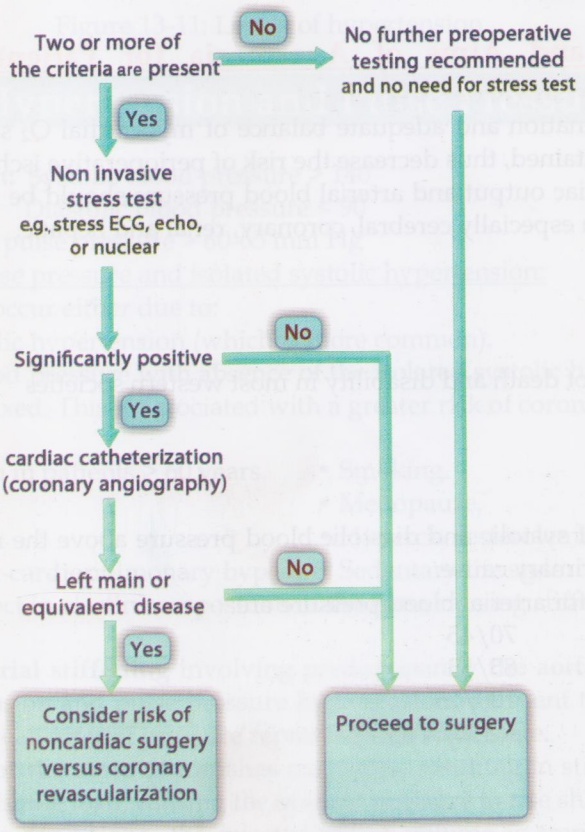


Figure 13-10: Assessment of the need of invasive or noninvasive cardiac tests

Three therapeutic options are available before elective non-cardiac surgery:

1- Revascularization by surgery (Coronary artery bypass grafting) (CABG).
2- Revascularization by percutaneous coronary intervention (PCI).
3- Optimal medical management.

Other Intraoperative Risk Factors

1- Wide hemodynamic variations.
2- Duration of surgery > 3 hours.
3- Type of anesthesia: Although the superiority of regional anesthesia over general anesthesia for patients with cardiovascular diseases might seem obvious, studies supporting this view are deficient. Moreover, the hemodynamic effects of spinal and epidural anesthesia may be more detrimental than well managed general anesthesia for some patients.
4- Inexperience of anesthesiologists, surgeons or assistants.
5- Lack of sufficient monitoring.

Other Postoperative Risk Factors

1- Pain relief.
2- Availability of high dependency care or an intensive care facility.
3- Anemia.
4- O_2 therapy.

N.B.: The highest risk periods during anesthesia include: - induction and intubation,
and - postoperative period.

Q: Discuss preoperative assessment of a patient with cardiac diseases?
A: The following items should be discussed.

- Perioperative cardiac risk factors.
- Preoperative assessment of a patient with hypertension, ischemic heart disease, and valve lesions (including exercise tolerance).

General Principles and Aims of Anesthesia for Patients with Cardiovascular Diseases:

1. Heart: Adequate oxygenation and adequate balance of myocardial O_2 supply to demand throughout anesthesia should be maintained, thus decrease the risk of perioperative ischemia and infarction.
2. Tissues: Adequate cardiac output and arterial blood pressure should be maintained to allow adequate tissue and organ perfusion especially cerebral, coronary, renal and hepatic.

Hypertension

It is the commonest cause of death and disability in most western societies

Incidence

1: 5 of all surgical patients.

Definitions

It is a sustained increase of systolic and diastolic blood pressure above the normal range for age, sex and weight regardless of the primary cause.
The accepted upper limits for arterial blood pressure are:

• Infants	70/45
• Childs	85/55
• Adolescents	100/75
• Adults	< 130/< 85

Levels and Categories of Hypertension

Category	Systolic Blood Pressure (mm Hg)	Diastolic Blood Pressure (mm Hg)
Optimal	< 120	< 80
Normal	< 130	< 85
High normal (prehypertension)	130-139	85-89
Hypertension (combined systolic and diastolic hypertension)		
• Non-sustained labile (borderline)	140-159	90-99
• Mild (stage I) (sustained)	140-159	90-99
• Moderate (stage II)	160-179	100-109
• Severe (stage III)	180-209	110-119
• Very severe (stage IV)	> 210	> 120
Stages II to IV are sustained.		
Isolated systolic hypertension	> 140	< 90
Pulse pressure hypertension	Pulse pressure > 60-65 mm Hg	
Isolated diastolic hypertension	< 140	> 90

The blood pressure should be measured on 2 occasions at least 1-2 weeks apart to diagnose hypertension (figure 13-11).

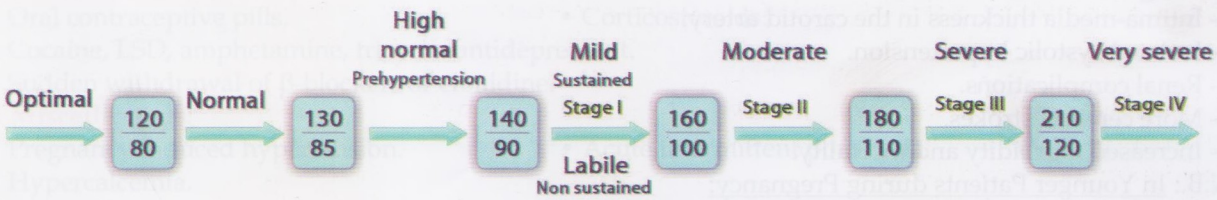


Figure 13-11: Levels of hypertension

Isolated Systolic Hypertension and Pulse Pressure Hypertension

Definition:

Isolated systolic hypertension: Systolic blood pressure > 140
Diastolic blood pressure < 90

Pulse pressure hypertension: pulse pressure > 60-65 mm Hg

The relation between high pulse pressure and isolated systolic hypertension:

Increased pulse pressure can occur either due to:

- Increased isolated systolic hypertension (which is more common).
- Decreased diastolic blood pressure with absence of the isolated systolic hypertension as the systolic blood pressure becomes fixed. This is associated with a greater risk of coronary ischemic events.

Precipitating Factors:

- Increasing age: It is common in patients > 60 years.
- Diabetes mellitus.
- Coronary artery diseases.
- Inflammatory response post-cardiopulmonary bypass.
- Genetic factors due to a defect in elastin composition in the aorta causing stiffening.
- Smoking.
- Menopause.
- Hypercholesterolemia and hyperlipidemia.
- Sedentary life style

Pathology:

- The main pathology is **arterial stiffening** involving predominantly **the aorta and its major branches**. The isolated systolic hypertension and pulse pressure hypertension represent the pulsatile component of blood pressure whereas the mean arterial pressure represents the static state.
- The net result **compliance of the aorta diminishes** markedly, resulting in stiffening of the arterial tree and inability to absorb the pulsatile load, causing the systolic pressure to rise sharply.
- **Under normal physiologic conditions**, the injected blood volume is transmitted peripherally as a **propagated pulse wave**. After reaching the periphery, in particular, at the bifurcation sites, **a reflected**

pulse wave or a retrograde pulse wave is generated; this travels toward the aortic valve. Arrival of this wave generally **coincides with the beginning of diastole**, thereby **augmenting the diastolic pressure**.

• **In patients with central aortic stiffening** (usually with precipitating factors such as aging), both the **propagated and the reflected waves** travel much **more rapidly**, and early return of the reflected arterial wave during late systole **augments the systolic components**, effectively increasing afterload. The ensuing **loss of diastole augmentation** results in a disproportionate increase in the systolic blood pressure with a lower diastolic blood pressure. This also **decreases organ perfusion** such as coronary, cerebral and renal vessels.

• This high pulse pressure produces repetitive pulsatile stress to which conduit vessels are exposed. This causes breakdown of the elastic elements producing vessel dilation and **more stiffening**.

Complications (and Risks) of High Pulse Pressure (i.e., increased vessel stiffness)

1- Atherosclerosis: as high pulse pressure may cause plaque rupture and increase atherosclerosis complications. **Systolic and pulse pressure hypertension are markers of** macrovascular disease and large arterial stiffening (atherosclerosis), while diastolic hypertension is a marker of microvascular diseases involving typically vessels less than 1 mm in size (arteriosclerosis).

N.B.: The difference between **atherosclerosis** (a patchy, mostly internal process mainly of large vessels) and **arteriosclerosis** (a diffuse involvement of the media mainly of small vessels) may have significant impact on overall mechanical properties of the vessel wall. It is possible to have one without the other.

2- Left ventricular hypertrophy.
3- Myocardial infarction.
4- Congestive heart failure.
5- Intima-media thickness in the carotid artery.
6- Isolated systolic hypertension.
7- Renal complications.
8- More cerebral strokes.
9- Increased morbidity and mortality.

N.B.: In Younger Patients during Pregnancy:

• Elevation in pulse pressure during the first trimester is important in predicting preeclampsia and eclampsia in the third trimester.

• Normally during pregnancy, pulse pressure increases because there is an increase in the intravascular volume, whereas the maternal vasculature cannot compensate for this increase in volume i.e., poor vascular compliance causing elevated pulse pressure.

Causes

The following causes are mainly to the **diastolic hypertension** or **combined systolic and diastolic hypertension.**

A) Essential (Primary) Hypertension:

It represents 90% of cases of hypertension. Chronic cases may cause hypertensive crisis (discussed later).

Pathophysiology:

The exact mechanism is still unclear, but there are derangements in the neuro-endocrine and autonomic systems. Hereditary factors may be involved. One of the following mechanisms may be the cause of the primary hypertension.

1- Increased renin-angiotensin-aldosterone activity.
2- Decreased Kallikrein-Kinin system activity: There is a decrease in Kallikrein enzymes released from the kidney (due to pathogenetic factor). This decreases production of bradykinin from kininogen (bradykinin has a vasodilatory property).
3- Vasopressin (anti-diuretic hormone): It is a potent vasoconstrictor, released in response to acute hypovolemia. It may play a role in volume-dependent forms of hypertension.
4- Hypothalamic natriuretic factor: It inhibits Na^+-K^+ ATPase, so an increase in intracellular Ca^{++} occurs. This increases arterial tone causing vasoconstriction.
5- Atrial natriuretic factor: It stimulates diuresis by inhibition of renin activity.
6- Abnormal increase in intracellular Na^+ can decrease renal excretion of Na^+.
7- Sympathetic over-activity with increased response to sympathetic agonists, vasopressors and stress response.

Initially, increased arterial blood pressure is associated with increased cardiac output, but systemic vascular resistance appears to be normal. Then as the disease progresses, cardiac output returns to normal, but systemic vascular resistance starts to increase markedly. Later on, cardiac output increases again.

B) Secondary Hypertension:

It represents 10% of cases of hypertension.

1. Renal:

- Renal artery stenosis (the most common cause of secondary hypertension).
- Chronic renal failure.
- Acute glomeruli-nephritis.
- Congenital polycystic kidney.
- Chronic glomeruli-nephritis.
- Chronic pyelonephritis.

2. Endocrinal:

- Cushing's disease and syndrome.
- Conn's disease.
- Pheochromocytoma.
- Acromegaly.
- Thyrotoxicosis.
- Myxedema.

3. Cardiovascular:

- Coarctation of aorta.
- Polyarteritis nodosa.

4. Neurogenic:

- Increased intracranial tension.
- Spinal cord section.
- Polyneuritis.
- Guillain Barré syndrome.

5. Pharmacological:

- Oral contraceptive pills.
- Corticosteroids.
- Cocaine, LSD, amphetamine, tricyclic antidepressant.
- Sudden withdrawal of β-blockers or clonidine.

6. Miscellaneous:

- Pregnancy induced hypertension.
- Acute intermittent porphyria.
- Hypercalcemia.

Treatment:

1- Treatment of the cause of secondary hypertension (if present).
2- Treatment of the risk factors such as obesity.
3- Pharmacological therapy:

- Mild hypertension is usually treated with single-drug therapy, but more severe hypertension may require a combination of drugs.
- Drug therapy includes:

  1- Diuretics: thiazide diuretics (recommended for all patients with hypertension), potassium sparing diuretics, or loop diuretics.

  2- Sympatholytics: β-blockers (especially for those with coronary artery diseases), α-blockers, α- and β- blockers, central α_2-agonists, or postganglionic blockers.

  3- Vasodilators: Calcium channel blockers, angiotensin-converting enzyme inhibitors (the first choice for patients with left ventricular dysfunction, heart failure, or diabetes mellitus), angiotensin-receptor blockers, or direct vasodilators.

These drugs are discussed in more details in chapter "Pharmacological Adjuncts to Anesthesia & Intensive Care".

Hypertensive Crisis

Definition:

It is typically a blood pressure of **higher than 180/120 mm Hg** and can be categorized as either:

- **Hypertensive urgency**: without impending or progressive target organ damage,

or • **Hypertensive emergency**: with evidence of impending, acute or ongoing **target organ damage** such as encephalopathy (with damage of blood vessels resulting in increased permeability and brain edema), intra-cerebral hemorrhage, acute left ventricular failure with pulmonary edema, unstable angina, dissecting aortic aneurysm, acute myocardial infarction, eclampsia, micro-angiopathic hemolytic anemia, or renal insufficiency.

Encephalopathy occurs when diastolic blood pressure exceeds 150 mm Hg except in pregnancy-induced hypertension, encephalopathy occurs when diastolic blood pressure exceeds 100 mm Hg.

Subtypes of Hypertensive Emergency:

• **Hypertensive encephalopathy**: is a hypertensive emergency characterized by irritability, headache, and mental status changes caused by significant and often rapid elevations in blood pressure.

• **Malignant hypertension**: is a hypertensive emergency with end organ damage namely encephalopathy, nephropathy, eye finding as retinal hemorrhage, exudates, or papilloedema.

• **Accelerated malignant hypertension**: is a hypertensive emergency characterized by fundoscopic findings of papilloedema and/or acute retinal hemorrhage and exudates.

Causes:

Any cause of hypertension either essential or secondary can produce hypertensive crisis.

Clinical Pictures and Investigations:

They are of **end organ damage** such as myocardial infarction, cerebral hemorrhage…etc.

Treatment and Intensive Care Considerations:

1- Immediate Management is required:

Drugs such as **nitroprusside** (the most important), labetalol, fenoldopam, nicardipine, nitroglycerin, trimethaphan, Mg sulfate, hydralazine, phentolamine, β-blockers, or enalaprilat (the only i.v. angiotensin-converting enzyme inhibitor) are used because they have a rapid onset of action and are easily titrated **with invasive blood pressure monitor and urine output**.

The following precautions should be taken:

• **Diastolic** blood pressure should be **decreased gradually** to avoid coronary or cerebral ischemia.

• Typically, **mean** blood pressure is **reduced by about 20% within the first 60 minutes** and then more gradually.

• Then blood pressure can be **decreased to 160/110 mm Hg over the next 2-6 hours** as tolerated by the absence of symptomatic hypoperfusion of target organs.

• After blood pressure is lowered to a satisfactory level, institution of **oral antihypertensive drugs** is begun with the goal of **discontinuing the nitroprusside within 24-48 hours**.

2- Treatment of the Cause.

Anesthetic Management of Hypertension

Preoperative Management (and Assessment): by (history-examination-investigations).

1. Decision Whether to Delay or to Proceed with Surgery:

• The decision should be **individualized** and it is based on:

1- The severity of the preoperative blood pressure elevation.

2- Presence of complications.

3- The type of surgery, if major changes in the preload or the afterload are expected.

• There is association between **preexisting untreated hypertension** and increased **risk of perioperative** blood pressure fluctuation during anesthesia, stroke, myocardial infarction, congestive heart failure, bleeding and renal dysfunction.

• In **younger patients (< 50 years)**, **diastolic blood pressure** is the most important risk factor for cardiovascular outcomes. It is more important than systolic blood pressure. In **elderly patients (> 50 years)**, **systolic blood pressure** is the most important (more than diastolic blood pressure) for predicting coronary heart diseases, congestive heart failure, strokes in perioperative period.

• Patients with moderate hypertension **(i.e., diastole < 110 mm Hg)** and not having any complications can undergo elective surgery. Actually, other anesthesiologists cancel cases if diastolic blood pressure is > 95-100 and systolic blood pressure > 160 mm Hg.

• The approach that the patient should be normotensive before elective surgery is not always feasible or necessarily desirable due to altered cerebral and renal autoregulation.

• Patients with **diastolic blood pressure > 110-115 mm Hg or isolated systolic hypertension > 200 mm Hg** should be **delayed (postponed)** until blood pressure is controlled over the course of several days. Acute control within several hours is not advised because it gives no time for resetting of cerebral or renal autoregulation (N.B.: sublingual nifedipine (*Epilat*) is associated with reported cases of severe hypotension and death; therefore, it should not be used).

2. Severity and Duration of Hypertension: should be assessed as above.

3. Cause and Type of Hypertension: should be assessed as above.

N.B.: Failure of diagnosis of pheochromocytoma preoperatively is proved fatal.

4. Complications of Hypertension:

Clinical pictures and investigations of each complication should be revised. Complications usually start to occur after 5-10 years and end up with **end organ damage** after 20 years. All organs should be assessed by **history, examination and investigations**.

1- Cardiac: cardiomegaly, left ventricular failure, arrhythmias, ischemia, and infarction.
2- Vascular: peripheral occlusive disease, and aortic dissection.
3- Neuronal: cerebrovascular accident (hemorrhagic, thrombotic), transient ischemic attacks, and hypertensive encephalopathy.
4- Renal: impairment.
5- Ophthalmic: hypertensive retinopathy; retinal changes parallel severity in other organs (by ophthalmoscopy).
6- Orthostatic changes: i.e., blood pressure should be measured in both the supine and standing positions as orthostatic changes can occur due to volume depletion (common), excessive vasodilators, or sympatholytic drug therapy. So, preoperative fluid administration can prevent severe hypotension after induction of anesthesia in these patients.

5. Preoperative Drugs Taken:

• The **side effects** of antihypertensive drugs taken should be assessed, for example, hypokalemia and hypovolemia are common findings with diuretics; therefore, preoperative fluid administration is important. See chapter of "Pharmacological Adjuncts for Anesthesia and Intensive Care".

• **Drug interaction** with anesthetic drugs should be evaluated. For example:
- Ca^{++} channel blockers with high doses of opioids may cause severe bradycardia.
- Reserpine and guanethidine may cause marked depletion of norepinephrine from sympathetic nerve endings. This results in exaggerated effects to inhalational anesthetic agents.

• **Continuation of drug therapy**: Antihypertensive drugs should be **continued up** to the time of surgery with a small sip of water. For example:
- Acute withdrawal of **β blockers** or centrally acting antihypertensive drugs e.g., clonidine may precipitate severe hypertension and ischemic attacks.
- Diuretics may be stopped 2 days before surgery to avoid dehydration as it increases the risk of postoperative renal impairment.
- Angiotensin converting enzyme inhibitors (ACEIs) may be stopped one day (the evening before surgery) as it increases the hypotensive response to induction agents, but this increases the risk of perioperative hypertension.
- Statins (drugs which decrease cholesterol level) should be given preoperatively, but the optimal timing is unknown. It has been suggested that statin therapy should be commenced 1 month preoperatively especially in patients with cardiovascular diseases such as coronary artery disease.

6. Premedications:

1. **Sedatives:** decrease preoperative anxiety such as midazolam. The blood pressure in some patients on admission to the hospital is increased (white coat syndrome), reflecting patient anxiety. After sedation, their blood pressures are typically decreased. Avoid over-sedation as it may cause hypoxemia, respiratory acidosis, and hypotension.
2. **Clonidine** 0.2- 0.3 mg: It acts as a sedative, decreases the anesthetic needs, and increases hemodynamic stability.
3. **Glycopyrrolate** is preferred (to atropine) as it produces less tachycardia.
4. **Prophylactic Transdermal Nitroglycerin:** decreases the incidence of ischemia theoretically, but clinically this has not been proved.

Intraoperative Management

Aim:

Arterial blood pressure should be maintained stable within 10-20% of preoperative level because marked variability leads to: - increased incidence of ischemia of myocardium.
- increased incidence of ischemia of cerebral and renal tissues due to altered auto-regulation which is reset to a higher level.

If there is markedly increased arterial blood pressure e.g., > 180/120 preoperatively, keep blood pressure in the high normal range $\frac{140\ \ 150}{80\ \ 90}$ mm Hg.

Monitoring:

It should be instituted before induction and maintained throughout the immediate postoperative period. It is chosen according to the complexity of the operation and medical condition of the patient. All these monitors are discussed in more details in the chapter of "Monitoring during Anesthesia and Intensive Care".

1. Arterial Blood Pressure Measurement:

- Non-invasive measurement is usually used.
- Invasive measurement: is used in the following conditions:
  - Patients with wide swings of blood pressure.
  - Major surgery with rapid or marked fluid shifts.
  - Patients on nitroprusside or nitroglycerin.

2. ECG:

- **CM_5 lead I** is chosen because it detects 80% of myocardial ischemia.
  - Lead II is chosen if inferior wall ischemia is suspected.
  - V5 lead is chosen if anterior and lateral wall ischemia are suspected.
  - Esophageal lead is used if posterior wall ischemia is suspected.
- Automated ST segment analysis monitors and trends are useful in these cases.

3. Pulse Oximetry: is used to detect peripheral blood flow and oxygenation.

4. End-Tidal CO_2: is used to maintain normocapnia.

In addition to other monitors:

5. Urine Output: is especially indicated in patients with renal impairment and undergoing surgery which lasts > 2 hours.

6. Central Venous Pressure Measurement.

7. Pulmonary Artery Pressure Measurement: is indicated in

- Patients with ventricular dysfunction or failure.
- History of recent myocardial infarction.
- Major vascular or cardiac surgery.

It is useful for measurement of:

- Pulmonary capillary wedge pressure to maintain it between 12-18 mm Hg. It reflects left ventricular end-diastolic volume and pressure. Both increase in global myocardial ischemia not in minor ischemia of left ventricle; therefore, it is an insensitive test.
- Cardiac output and assessment of the efficacy of treatments such as inotropes.
- Sampling of pulmonary arterial blood for mixed venous blood saturation ($S\bar{v}O_2$). Fiberoptic pulmonary artery catheter (the most practical intraoperatively) allows continuous monitoring of $S\bar{v}O_2$.

8. Two-Dimensional Trans-Esophageal Echocardiography:

It is more sensitive than ECG. It is indicated in patients suspected to have myocardial ischemia. It can detect - new regional wall motion abnormalities (occur before ECG changes),

- reduction of systolic wall thickening,

and - ventricular dilatation.

It is expensive, needs extensive training, and is inserted only after induction of anesthesia.

Choice of Anesthesia:

A. Regional Anesthesia:

It is accepted because it avoids the stress response of intubation.

It is used with care to:

- avoid hypotension by prior volume loading, ephedrine, phenylephrine, or even epinephrine in severe cases because hypotension may cause myocardial ischemia.
- avoid patchy or incomplete anesthesia because it increases the patient's stress and increases blood pressure and ischemia.
- avoid adrenaline containing local anesthetics because they increase arterial blood pressure and ischemia.

Sympathetic block is beneficial in the following conditions:

- Compensated congestive heart failure as it decreases the afterload.
- Peripheral vascular disease as it causes vasodilatation.

B. General Anesthesia:

Induction:

• Hypertensive patients display accentuated hypotensive response to induction of anesthesia followed by accentuated hypertensive response to intubation.

• The pressor response to laryngoscopy and intubation should be reduced for example, additional doses of opioids. The methods for reduction of the pressor response are discussed in full details in chapter "Airway Management".

• Intubation via Fastrach laryngeal mask airway is associated with a less pressor response than intubation with direct laryngoscopy.

• Induction agents: after good preoxygenation such as:

- Large doses of opioids and an appropriate muscle relaxant with etomidate (has the least cardiovascular effect) are advised.
- Thiopentone and propofol can be used, but only a sleeping dose as both cause significant cardiovascular depression.
- Ketamine is contraindicated due to the associated increase in heart rate and systemic blood pressure and transiently increases myocardial oxygen requirements.

Maintenance:

According to the Cardiovascular Function of the Patient;

• In patients with good ventricular function (i.e., ejection fraction > 50%), volatile based anesthesia is used. This is usually done in hypertensive patients only or those with slight cardiac injury.

• In patients with bad ventricular function (i.e., ejection fraction < 50%), opioid based anesthesia is used.

Volatile Agents:

A small concentration helps to:

- decrease arterial blood pressure and allows control of intraoperative rise of blood pressure.
- produce controlled myocardial depression to decrease the oxygen needs.
- produce preconditioning of the myocardium to tolerate subsequent ischemic events.

• **Halothane:** It slightly decreases coronary blood flow and moderately decreases myocardial contractility; therefore, it can be used.

• **Isoflurane:** It has no effect on coronary blood flow and slightly decreases myocardial contractility; therefore, **it is the best** agent used (although there is a possibility of coronary steal phenomenon, but this is not important clinically).

• **Sevoflurane**: **It is used safely.**

• **Enflurane:** It slightly decreases coronary blood flow, but markedly decreases myocardial contractility, therefore; **it is better avoided.**

• **Desflurane:** It increases the heart rate resulting in increased O_2 demand; therefore, **it is not preferred.**

Opioids: are of choice as they do not affect blood pressure (if used alone).

Alfentanil and sufentanil are more effective than fentanyl in preventing intraoperative rise of arterial blood pressure and heart rate.

N_2O:

• N_2O alone (even < 40%) produces small, but significant myocardial depression.

• N_2O with opioids produces marked myocardial depression resulting in decreased cardiac output and blood pressure.

• N_2O in patients with pulmonary hypertension, pulmonary vasoconstriction is produced resulting in increased pulmonary vascular resistance.

Generally, N_2O is used safely in patients with hypertension, but N_2O with opioids is better avoided in patients with ischemic heart disease.

Muscle Relaxant:

• Vecuronium, rocuronium, cis-atracurium, doxacurium, and pipecuronium are of choice.

• Pancuronium slightly increases heart rate and blood pressure, but if it is used in a small dose and injected slowly, it can be safe.

• D-tubocurarine, alcuronium, and atracurium may cause histamine release which may cause a severe transient fall in blood pressure, but if atracurium is used in a small dose and injected slowly, it can be safe.

Reversal of Muscle Relaxants:

Glycopyrrolate is preferred (instead of atropine) to decrease the effect on heart rate.

Mechanical Ventilation:

• It should maintain normocapnia ($PaCO_2$ between 35-40 mm Hg) as hypocapnia causes:

- Respiratory alkalosis which causes 2ry hypokalemia. Therefore, arrhythmia (especially nodal) may occur.
- Peripheral vasoconstriction and myocardial depression which increase the systemic vascular resistance and decrease the stroke volume. Therefore, increased arterial pressure and decreased cardiac output may occur.
- Coronary artery vasoconstriction.

• In hypovolemic patients, arterial blood pressure may decrease significantly.

Intraoperative Complications:

1. Intraoperative Hypertension:

• At first, exclude hypoxia or hypercapnia.

• Secondly, increase the depth of volatile agents; if failed, use one of the following drugs:
- Nitroprusside or nitroglycerin: They need invasive blood pressure monitoring. They are the most effective drugs.
- Hydralazine, nifedipine, and trimethaphan.
- Propranolol, esmolol, and labetalol: They are contraindicated in asthmatic patients.

2. Intraoperative Hypotension:

At first, decrease the depth of volatile agents. If failed; use one of the following methods:
- Increased i.v. fluid rate.
- Ephedrine or phenylephrine i.v.: Give the smallest dose and in increments because there is an exaggerated response to vasopressors in hypertensive patients.

3. Intraoperative Dysrhythmias:

The commonest is nodal dysrhythmias (especially with hypokalemia).

• At first, decrease the concentration of volatile agents (especially halothane).

• Avoid hypocapnia.

• Then according to the heart rate, use either i.v. atropine or β blockers.

4. Intraoperative Ischemia:

• At first, increase O_2 supply by correcting hypotension, hypoxemia, and anemia (hematocrit < 28% is associated with a high incidence of perioperative ischemia) and decrease O_2 demand by correcting hypertension, and tachycardia.

• Secondly, use nitroglycerin i.v. drip, patch or paste, or i.v. nicardipine.

5. Intraoperative Blood Loss:

These patients are more vulnerable to small changes in the blood volume due to:
- The decreased left ventricular compliance and rigid atherosclerotic vascular tree.
- β-blockers used in treatment of hypertension can prevent the physiological heart rate response to blood loss.
- Vasodilators used in treatment of hypertension can prevent the physiological vasoconstriction response to blood loss.

Therefore, careful monitoring with central venous pressure measurement and prompt replacement are essential.

Application of Elective Controlled Hypotensive Anesthesia in Hypertensive Patients

• In untreated or uncontrolled severe hypertension, elective hypotension is contraindicated.

• **In treated hypertension**, elective hypotension is used cautiously. Blood pressure can be decreased as follows: a. **Decrease the mean arterial blood pressure up to 25%**. This coincides with the lower limits of cerebral autoregulation.

Decreasing the mean arterial blood pressure up to 55% coincides with symptomatic cerebral hypoperfusion.

or b. Systolic blood pressure of elective hypotension should not be lower than the diastolic blood pressure of the patient's usual pressure.

Because, in chronic hypertension, cerebral autoregulation is reset to a higher level and may not return to the normal range after treatment.

Recently, noninvasive **cerebral oximeter** can be used to determine the O_2 saturation of cerebral cortex and thus can determine the lower limit of autoregulation and hence elective hypotensive level.

Recovery and Extubation:

Recovery and extubation should be smooth and the stress response of extubation should be decreased by giving 2 min before extubation one of the following drugs: lidocaine 1.5 mg/kg iv, diltiazem 0.1 mg/kg iv, or verapamil 0.1 mg/kg i.v.

Postoperative Management:

Close monitoring of patients to avoid **postoperative hypertension** is required. It increases the risk of ischemia, congestive heart failure or wound hematoma.

The possible causes of postoperative hypertension: pain (the most common),
volume overload,
bladder distension,
hypothermia (it produces vasoconstriction),
and respiratory distress (hypoxia or hypercarbia).

Treatment:

- Treatment of the cause e.g., analgesics for pain, urinary catheter…etc.
- Antihypertensive agents if hypertension persists.

On resuming oral intake, restart oral antihypertensive therapy.

Reno-Vascular Hypertension

It is the most common cause of secondary hypertension. It is one of the surgically corrected hypertensions.

Incidence: 2-5% of all cases of hypertension.

N.B.: Surgically corrected causes of hypertension include:

- Reno-vascular hypertension (treated either surgically or by angioplasty).
- Cushing disease and syndrome (treated by adrenalectomy).
- Conn's disease (treated by adrenalectomy).
- Coarctation of the aorta (treated by surgical repair).
- Pheochromocytoma (treated by surgical excision).

Pathophysiology:

Uni- or bilateral stenosis of the renal artery decreases the perfusion pressure of the kidneys distal to the obstruction. This stimulates the juxta-glomerular apparatus, with subsequent increased renin release which results in an increase in angiotensin II.

The release of angiotensin II increases the systemic vascular resistance and aldosterone secretion which in turn, increases Na^+ retention. Therefore, the net result is systemic hypertension.

Causes of Stenosis:

1- Atheromatous plaque in the proximal renal artery (2/3 of cases): It is common in men > 55 years.

2- Malformation of the renal artery (fibro-muscular hyperplasia or dysplasia) (1/3 of cases): It is common in women < 35 years.

3- Less common causes: dissecting aneurysm,
emboli,
polyarteritis nodosa,
radiation,
trauma,
hypoplasia of the renal artery,
or external compression from retro-peritoneal fibrosis or tumors.

Clinical Pictures and Investigations: Age < 35 ♀ or > 55 ♂

1- **Hypertension** either of a sudden onset or suddenly accelerated or malignant hypertension if the patient is already hypertensive.

2- Secondary hyper-aldosteronism which may cause:
- Na retention which leads to **edema formation**.
- **Metabolic alkalosis**.
- **Hypokalemia** which leads to **muscle weakness**.
- **Polyuria and tetany**.

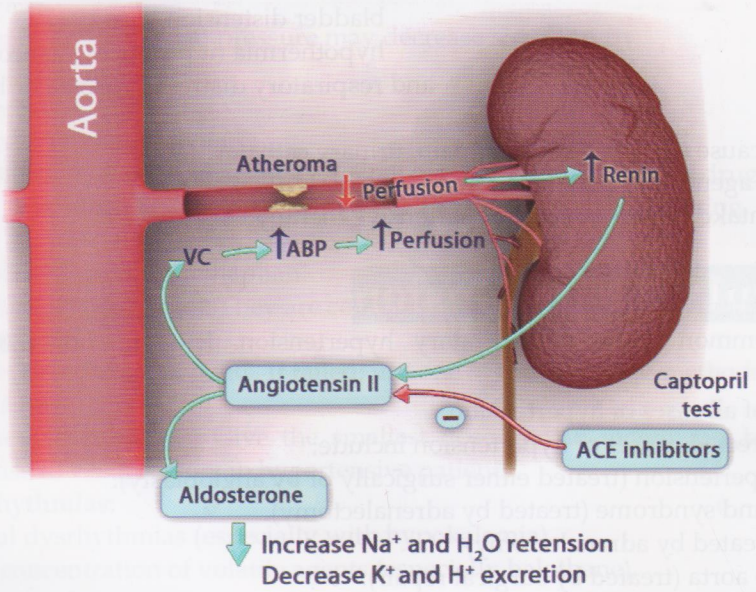
3- A mid-abdominal **bruit**.

4- **Captopril test** (it is a good screening test): It depends on administration of captopril (one of the ACEIs) (figure 13-12). It causes persistent decreased renal perfusion detected by an isotope scan in these patients. If it is positive, do one of the following tests:

- digital subtraction angiography to detect the stenosis (figure 13-13),

or - rapid sequence i.v. pyelogram.

5- **Selective catheterization of both renal veins** to measure plasma renin from each kidney. It is typically increased in the stenotic side. Patients with renal artery stenosis with a plasma renin activity ratio on both sides > 1.5: 1 have greater than 90% cure rate after surgery. Giving ACEIs greatly magnifies the difference between the two sides. If the stenosis is bilateral, the ratio may be < 1.5: 1, but the patient may still benefit from surgery.



ABP Arterial Blood Presure
ACE Angiotensinogen Converting Enzyme
VC Vasoconstriction

Figure 13-12: The captopril test

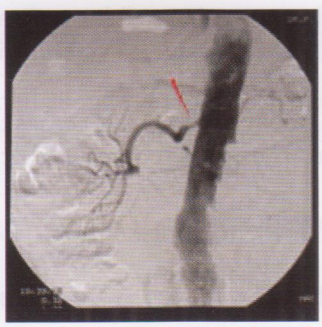


Figure 13-13: Digital subtraction angiography of a renal artery showing narrowing near its origin from the aorta (arrow)

Anesthetic Management:

Preoperative Management:

Patient Preparation:

1. Control arterial blood pressure to be within a normal range by:
   - ACEIs: Only enalaprilat is available in the i.v. form. It is used only preoperatively.
   - β blockers: They are used pre-, intra- and postoperatively. They are effective because renin secretion is mediated by β_1 receptors. For example: propranolol or esmolol (of choice) because it is a selective β_1 blocker and it has a short $t_{1/2}$; so, it can be titrated.
   - Centrally acting sympathetic blockers.
   - Direct vasodilators e.g., nitroprusside, nitroglycerin (used only intraoperatively).
   - Saralasin (angiotensin II blockers): Its use is limited because it has a partial agonist activity.
2. Correct metabolic disturbances e.g., hypokalemia or alkalosis.
3. Evaluate renal function.
4. Evaluate coexisting atherosclerotic disease especially of coronary arteries in > 50 years old male.

Intraoperative Management:

Anesthetic Problems:

1. Major blood loss and fluid shifts:

Surgical correction includes:

- Trans-aortic renal endarterectomy.
- Aorto-renal bypass (using a saphenous vein, synthetic graft, or a segment of the hypogastric artery).
- A splenic to left renal artery bypass.
- A hepatic or gastro-duodenal to right renal artery bypass.
- Excision of the stenotic segment with re-anastomosis of the renal artery to the aorta.
- Rarely nephrectomy.

Heparinization is needed. It increases blood loss.

Therefore, all measures to decrease blood loss should be taken e.g. wide bore i.v. cannulas …etc.

2. Aortic cross-clamping:

May be required; therefore, invasive intra-arterial blood pressure, central venous pressure, pulmonary artery pressure, urine output may be measured in patients with bad ventricular function.

3. Measures to protect the affected and normal kidney from the ischemic injury such as:

- Generous hydration.
- Osmotic diuresis e.g., mannitol.
- Topical cooling of the affected kidney during anastomosis.

Anesthetic Technique:

It depends on the patient's cardiovascular function as discussed before in hypertension.

Postoperative Management:

Close monitoring is essential in the early postoperative period because blood pressure is still labile during this period.

Ischemic Heart Disease

Myocardial O_2 demand exceeds its O_2 supply.

Causes:

Factors affecting O_2 balance such as increased contractility, increased heart rate, elevated blood pressure…etc are discussed before.

Risk factors for disease development

- Hypertension.
- Hyperlipidemia and hypercholesterolemia.
- Positive family history.
- Sedentary life.
- Diabetes mellitus.
- Advanced age.
- Menopause female patients.
- High estrogen containing oral contraceptive pills.
- Cigarette smoking.
- Male gender.
- Obesity.

Clinical Presentations of Ischemic Heart Diseases

Patients with ischemic heart diseases can present with:

1- Chronic stable angina (angina pectoris).

2- Acute coronary syndrome (with ischemic type chest pain): It includes one of the following clinical conditions:

a- ST-segment elevation myocardial infarction (with positive troponin/creatine kinase myocardial bound "CK-MB").

b- Non-ST- segment elevation (non-Q wave) myocardial infarction (with positive troponin/CK-MB).

c- Unstable angina; if troponin/CK-MB is negative (figure 13-14).

Chronic Stable Angina (Angina Pectoris)

It refers to chest pain or discomfort that does not change appreciably in frequency or severity over months or longer.

Clinical Picture:

1- Patient discomfort or pain: The patient may complain of either:

- Pain.
- Discomfort: as - heavy, pressure-like sensation.
  - choking or a constricting feeling in the throat.
  - indigestion or a sensation of strangling.
- It may be silent (especially in diabetes mellitus).

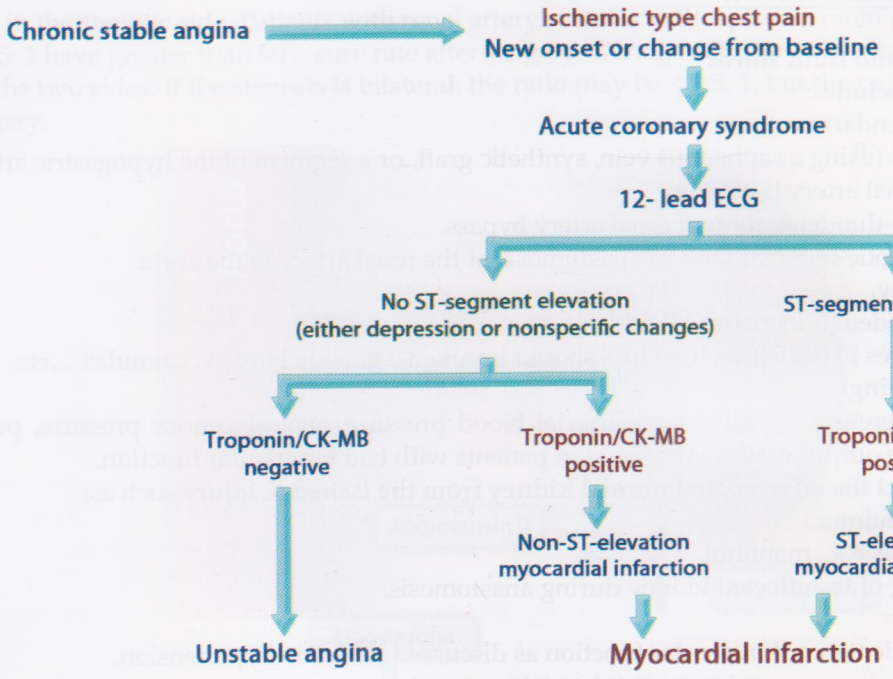


Figure 13-14: Presentation of ischemic heart diseases

2- Location: The pain or discomfort is usually located in one of the following areas:
- Substernal area (the most common) or retrosternal area.
- The arm (the left more often than right).
- The jaw, the neck, the left infrascapular region or occasionally, the epigastrium.

Pain of myocardial ischemia is not likely to be localized with one finger to a single point.

3- Duration:
- Pain of angina pectoris usually lasts 30 seconds to 15 minutes.
- Longer episodes of ischemic pain are associated with unstable angina or myocardial infarction.

4- Provocation: Pain or discomfort is induced by:
- Physical exertion • Emotional distress • Eating • Cold weather • and Sexual activity.

5- Relief: Pain or discomfort is relieved by:
- Rest or even a reduction in exertion.
- Sublingual nitroglycerin which relieves angina within 1-2 minutes.

6- Signs: During an episode of angina; one of the following can occur; S_3 gallop, pulmonary rales, or the murmur of mitral regurgitation.

Pathology:

It typically develops in the setting of partial occlusion or chronic narrowing of a segment of coronary artery.

- **Atherosclerosis**: is the most common cause.

Symptoms occur when atherosclerotic lesions cause 50-75% occlusion in the coronary circulation. When the stenotic segment reaches 70% occlusion, maximal compensatory dilatation is usually present distally resulting in adequate blood flow at rest, but becomes inadequate with increased metabolic demands e.g., during exercise. Collaterals occur in some patients. They make them asymptomatic in spite of severe disease.

- **Coronary vasospasm (vasospastic, variant, or prinzmetal's angina)**: 90% of vasospasm occurs at preexisting stenotic lesions in epicardial vessels and are usually precipitated by emotional upset or hyperventilation. It may occur at rest and then be come absent during vigorous exertion.

Differential Diagnosis of Chest Pain:

1- **Chest wall pain**: is often exacerbated by chest wall movement and associated with tenderness over the involved area, which is often a costochondral junction.

2- **Pericarditis**: It produces sharp retrosternal pain exacerbated by deep breathing, coughing, or change in body position.

3- **Esophageal spasm**: Its pain is related to meals and swallowing and can produce severe retrosternal pressure that may be confused with angina pectoris and may be **relieved by** administration of **nitroglycerin** (a smooth muscle relaxant).
4- **Aortic dissection**: The pain is classically "tearing" in quality and radiating to the back; pulses in the arms may be unequal.
5- **Gastrointestinal pain**: from esophagitis, gastritis, cholecystitis, and cholelithiasis (often associated with meals and relieved by antacids in case of esophagitis and gastritis).

Treatment:

1- Correction of risk factors to decrease disease progression.
2- Modification of the patient's life style to decrease stress and increase exercise tolerance.
3- Therapy to decrease myocardial O_2 consumption (demand):
• β-blockers: are of choice in exertional angina.
4- Therapy to increase myocardial O_2 supply:
• Coronary vasodilators:
  ▫ Ca^{++} channel blockers: are of choice in vasospastic angina.
  ▫ Nitrites: are of choice in both exertional and vasospastic angina.
  ▫ Angiotensin-converting enzyme inhibitors (ACEIs): are indicated in all patients with coronary artery diseases, especially those with hypertension, left ventricular dysfunction, or diabetes.
  ▫ Angiotensin II receptor blockers such as valsartan: are used in patients intolerable to ACEIs.

Most patients with stable ischemic heart disease are managed pharmacologically.
• Interventional therapy:
  ▫ Percutaneous trans-luminal coronary angioplasty: is indicated in one or two vessel coronary obstruction especially in discrete, concentric, proximal, non-calcified obstruction and less than 5 mm in length.
  ▫ Coronary artery bypass surgery: is indicated in significant left main or three-vessel coronary artery obstruction especially of reasonable size, has a high-grade proximal stenosis, and is free of significant distal plaques.

5- Antiplatelet therapy: Low-dose aspirin (75-325 mg/day), clopidogrel, ticlopidine, abciximab, eptifibatide, and tirofiban are useful in decreasing ischemic events especially after placement of an intra-coronary stent.

Acute Coronary Syndrome

Acute coronary syndrome represents a hypercoagulable state. Focal disruption of an atheromatous plaque triggers the coagulation cascade with subsequent generation of thrombi and partial or complete occlusion of the coronary artery leading to ischemic chest pain. ECG and cardiac enzymes are used to differentiate between different types of acute coronary syndrome.
• **ST-elevation myocardial infarction (STEMI)** (± Q-wave infarctions).
• **Non ST-elevation myocardial infarction (non-STEMI)** (non-Q-wave).
• **Unstable angina**.

Pathology:

• STEMI is due to complete and sustained thrombotic coronary occlusion.
Non-STEMI (infarction) and unstable angina (ischemia) are due to either:
  - partial thrombotic coronary occlusion,
  or – transient complete occlusion with spontaneous revascularization.
• **If the ischemia lasts more than 3-6 hours**, irreversible myocardial necrosis (i.e., non-STEMI) occurs.
• In all these conditions, **acute coronary thrombosis** is the main cause (therefore, therapy is directed now to prevent its occurrence such as antiplatelet therapy, anticoagulant therapy, chemical dissolution of clot by fibrinolytic agents and mechanical disruption of clots by coronary angioplasty). Other rare causes of coronary occlusion are acute coronary spasm and coronary artery embolization.
• The nidus for thrombus formation is **rupture of an atherosclerotic plaque**, which exposes the blood to thrombogenic lipids and leads to **activation of platelets** (which release thromboxane A_2, the latter produces more platelet aggregation and vasoconstriction) **and clotting factors**.
• The trigger for plaque disruption is not known, but liquefaction caused by local inflammation and inflammatory mediators is believed to be involved. Hydraulic stresses may also cause plaque rupture.

A) ST-Elevation Myocardial Infarction (STEMI) (+/- Q-Wave Infarctions):

Clinical Picture:

At least two criteria of the following three criteria should be present:

1- Chest pain: is the same as that of angina pectoris, but more severe, of longer duration, lasts from 10-15 minutes to several hours, and is not responsive to nitroglycerin and may require morphine for relief. The patient usually has fatigue, sweating, indigestion, nausea, syncope, and fever, and appears anxious and pale.

2- Serial ECG changes indicate myocardial infarction.

3- An increase of serum cardiac enzymes.

Complications:

- Anterior wall infarction stimulates the sympathetic system resulting in hypertension, premature ventricular contractions, tachycardia, atrial fibrillation, up to ventricular fibrillation.
- Inferior wall infarction stimulates the parasympathetic system resulting in hypotension, bradycardia, up to complete heart block.
- Congestive heart failure.
- Pericarditis and pericardial effusion.
- Ventricular septal rupture may occur in 0.5-1% which needs surgical repair.
- Mitral regurgitation due to papillary muscle infarction.
- Cardiac rupture may occur in 2-3% of cases after 3-10 days from the initial infarction.
- Sudden death may occur.

Treatment:

A- **Pain Relief Measures**: usually by

- i.v. morphine (2 mg increments) and/or
- sublingual nitroglycerin tablets or spray. It can be taken as an outpatient treatment. Sublingual tablets (usually 0.3 mg) can be repeated every 3-5 minutes (if pain persists) up to 3-5 tablets. More tablets can be given once blood pressure monitoring is available and the patient has no significant side effects such as dizziness or severe headache.
- i.v. or oral midazolam for sedation.

B- **After Hospitalization usually in Intensive or Coronary Care Unit**:

1- **Oxygen therapy**.

2- **Low dose aspirin one tablet,**
or clopidogrel 75 mg for those intolerant to aspirin or who have aspirin-allergy or patients already taking prophylactic aspirin.

3- **Reperfusion Therapy**:

- **I.v. nitroglycerin**: is given and the dose is increased gradually until pain relief or systolic blood pressure is decreased < 90-100 mm Hg.
- **Thrombolytic therapy**: e.g., streptokinase, tissue plasminogen activator, reteplase, or tenecteplase.

- It is indicated **if invasive therapy is not available** or **within the first 6 hours** and **maximally within less than 12 hours** from the onset of chest pain.
- They are contraindicated in patients with intracranial neoplasm, geriatrics > 75 years due to increased risk of intracranial hemorrhage, patients with risk of hemorrhage such as gastrointestinal ulcers, stroke, or aneurysm, day zero or one postoperatively (they can be used after 5 days postoperatively). Thrombolytic therapy is not recommended in patients with unstable angina or non-STEMI.
- After thrombolysis, patients should receive anticoagulants (heparin) **for 2 days** as follows:
  - Unfractionated heparin: Start with i.v. 60-70 unit/kg followed by 12-15 unit/kg/hour and keep aPTT 1.5-2 times control.
  - Low-molecular weight heparin (LMWH) such as enoxaparin i.v. 40 mg bolus followed by subcutaneous 1 mg/kg/12 hours (decrease the dose in renal insufficiency).
  - **Direct thrombin inhibitors** such as **bivalirudin** can be used instead of heparin in patients with heparin induced thrombocytopenia.

- **Primary coronary angiography and percutaneous trans-luminal balloon coronary angioplasty**:

It is the preferred reperfusion therapy. Ideally, it should be performed 90 minutes of arrival at the health care facility and **within 12 hours of symptoms onset**.
It should be followed by antiplatelet therapy and low-dose aspirin.

- **Emergency surgical revascularization**.

4- **Adjuvant Medical Therapy:**

• **Early β-blockers** can decrease the infarct size by decreasing heart rate, blood pressure, and myocardial contractility and should be continued indefinitely in all patients unless there is a contraindication.

• **Angiotensin converting enzyme inhibitors (ACEIs) or angiotensin II blockers** can be used in patients with large anterior myocardial infarction or in diabetic patients.

B) Unstable Angina/Non-ST-Elevation Myocardial Infarction (Non-STEMI) (Non-Q-Wave Infarction):

Clinical Picture:

The signs and symptoms of unstable angina and non-STEMI are the same as those of stable angina pectoris, and the distinction between them is in the three main presentations which are:

1- **Angina at rest or at minimal exertion** (usually lasts less than 20 minutes).

2- **An increase in the severity, frequency, or duration** of previously chronic stable angina (**crescendo angina**) or **new-onset angina** which is severe, prolonged or disabling.

3- **Hemodynamic instability or congestive heart failure** (signs of congestive heart failure include S_3 gallop, jugular venous distension, pulmonary rales, peripheral edema) or **ischemia-induced papillary muscle dysfunction** causing acute mitral regurgitation.

Treatment:

It is similar to STEMI; hospitalization, oxygen therapy, analgesia, β-blockers, sublingual nitroglycerin, anticoagulants, antiplatelets, primary angioplasty, and emergency surgical revascularization especially for patients with recurrent ischemic pain.

Anesthetic Management

Preoperative Management (and Assessment):

Prediction and risk assessment of a cardiac patient (risk stratification) is discussed above.

1. Decision Whether to Delay or to Proceed with Surgery (i.e., detect the Last Attack):

The incidence of perioperative heart infarction is:

All surgical patients	0.2%
History of coronary artery bypass surgery	1.2%
Previous myocardial infarction (MI) > 6 months	6%
Recent myocardial infarction 3-6 months	15%
Myocardial infarction < 3 months	30-40%

a- Traditionally, elective surgery should be **postponed** until at least **6 months after the last infarction** unless it is an emergency. With improvement of thrombolytics, angioplasty after acute MI, this time interval has decreased.

The American heart Association /American College of Cardiology Task Force: recently, they use **MI < 6 weeks** as the group at highest risk, while after that period the risk is based upon the presentation of the disease and exercise tolerance.

b- Patients undergoing percutaneous coronary intervention (PCI) (angioplasty):

• **Elective non-cardiac surgery** should be **delayed (postponed) for:**

4-6 weeks after coronary angioplasty.

6 weeks after percutaneous coronary intervention with **bare metal stent placement,**

and **12 months after drug-eluting stent placement** (some recommend at least 3 months for sirolimus drug eluting stents and at least 6 months for paclitaxel drug-eluting stents, see later).

This period is needed to allow complete endothelialization of the stent and completion of the dual antiplatelet therapies (aspirin and selective ADP receptor antagonists such as clopidogrel or ticlopidine). Stent placement (drug eluting or bare metal stents) is routinely followed by post-procedure antiplatelet therapy (for 6 weeks after bare metal stents and for 6-12 months after drug-eluting stents) to prevent acute coronary thrombosis and maintain long-term patency of the vessels. Therefore, the date, kind of stent, and any stent-related complications should be considered preoperatively.

• **For emergency non-cardiac surgery,** when delaying the surgery is not possible, patients can either **continue their antiplatelet** regimen **or** change to a **low molecular weight heparin** regimen. In either case, the risk of bleeding needs to be balanced with the risk of thrombosis.

Discontinuing or modifying antiplatelet therapy should involve a multidisciplinary team of cardiologist, surgeon, and anesthesiologist. The procedure, especially if emergent or urgent, should ideally be

performed in a center with interventional cardiology so that complications of stent thrombosis can be addressed promptly.

N.B.: Drug-Eluting Stents:

They differ according to the drug coating the stents:

- a chemotherapy agent; Sirolimus.
- an anti-metabolic agent; Paclitaxel.

Advantages: These agents prevent or delay re-stenosis and are more beneficial in certain patients such as diabetics.

Disadvantages:

- Allergic reactions can occur.

- It causes delayed re-endothelialization which requires dual antiplatelet therapies for at least 1 year (some recommend it for many years or even for a lifetime); therefore, it is recommended to postpone elective surgeries for months.

c- Preoperative Detection of Unstable Cardiovascular Diseases:

Patients with **acute disease as unstable** angina, or decompensated congestive heart failure of an ischemic origin are at a great risk. Therefore, elective surgery should be **postponed** until this unstable disease is resolved e.g., by drugs or trans-cutaneous angioplasty. Only emergency surgery is done.

d- Preoperative Detection of Patient's Need for Further Diagnostic Evaluation and Management:

- Patients with dyspnea or angina on mild exertion **(class III and IV)** need further investigations to decide further management. These patients should be **postponed.** Most patients with stable angina or angina on extreme exertion do not need further investigations as it does not change the anesthetic management.
- **Coronary artery bypass grafting (CABG) surgery**: The indications for preoperative coronary revascularization are the same as those in the non-operative setting. There is no value in perioperative coronary intervention in patients with stable ischemic heart diseases.
- **Percutaneous coronary intervention (PCI):** Angioplasty before elective non-cardiac surgery could improve outcome. Patients undergoing PCI should be postponed as above.

2. Detection of the Severity of Angina: is performed by history of **exercise tolerance.**

It is one of the most important determinants of perioperative risks and the need for invasive monitoring.

N.B.: The Canadian Cardiovascular Society Classification of Angina Pectoris:

It describes the amount of effort needed to produce angina pectoris.

Class I: Ordinary physical activity e.g., walking or climbing stairs.

Angina occurs with strenuous, rapid or prolonged exertion.

Class II: Slight limitation of ordinary activity.

Angina occurs with walking, climbing stairs rapidly, walking uphill, after heavy meals, in the cold, or wind, or under emotional stress for few hours.

Class III: Marked limitation of ordinary activity.

Class IV: Inability to do any physical activity as angina occurs at rest.

3. Correction of Possible Risk Factors.

4. Complications of Ischemia: should be detected and managed such as:

- Dysrhythmias.
- Congestive heart failure.

5. Other Coexisting Diseases: such as peripheral vascular disease, cerebral vascular diseases, seizures, and respiratory diseases as chronic obstructive pulmonary diseases should be detected and managed.

6. Preoperative Drugs Taken:

a- All antianginal treatment should be **continued perioperatively** including the time of surgery.

- **Nitroglycerin**: Although it should be continued perioperatively if was used as an active treatment, prophylactic administration is not efficacious in reducing perioperative cardiac morbidity and mortality.
- **β-blockers**: are effective in reducing perioperative cardiac morbidity and mortality. The heart rate should be kept around 60 beats/min. They should be administered for:
  - Patients undergoing high- or intermediate risk surgery.
  - Patients with a major clinical risk factor or multiple moderate clinical risk factors.
  - Patients with positive ischemia on the preoperative stress testing.

Abrupt withdrawal of β-blockers may cause increased heart rate and hypertension due to upregulation of receptors.

Excessive bradycardia should be treated with atropine, glycopyrrolate or isopreternol.

b- **α_2 agonists** such as clonidine decrease perioperative cardiac injury.

c- **Angiotensin-converting enzyme inhibitors (ACEIs)** should be **stopped for 24 hours** before surgery involving significant fluid shifts or blood loss as they may produce significant hypotension with general anesthesia,

d- **Antiplatelet therapy** as aspirin, clopidogrel, or ticlopidine should be **continued perioperatively especially in emergent surgeries**, but they preclude neuraxial anesthesia.

7. Preoperative Investigation:

1. ECG shows the following findings:

- Pathologic Q wave (> 1 mm wide) indicates old infarctions. It may or may not occur after STEMI by variable periods. If it occurs, it indicates a worse prognosis. It is present in:
  - Anterior wall: L_I and aVL + V_1 and V_2 → Anteroseptal (occlusion of left anterior descending artery).
    or + V_3 & V_4 → Strictly anterior (occlusion of left anterior descending artery).
    or + V_5 & V_6 → Anterolateral (occlusion of left anterior descending artery or left circumflex artery).
  - Inferior wall: → $L_{II, III}$ and aVF (occlusion of right coronary artery).
- Poor R wave progression.
- The ST segment shows one of the following:
  - A transient depression indicates subendocardial ischemia (classic angina).
  - A persistent depression indicates subendocardial infarction.
  - A transient elevation indicates transmural ischemia (variant angina).
  - Non-specific changes.
- T wave inversion occurs during ischemia.
- Long QT interval (QTc > 0.44 seconds).
- Dysrhythmias or heart block.

ECG traces are discussed in the appendix of this book.

2. Holter (Continuous Ambulatory) ECG Monitor: to evaluate:

- The severity and frequency of ischemic episodes.
- Silent ischemia.
- Dysrhythmias and anti-arrhythmic drugs.

3. Exercise ECG:

Type of exercise: Exercise is performed either by bicycle or treadmill. There are two types of exercise tests:

- **An ordinary** exercise stress test: is used for patients with **stable angina** with ordinary exercise levels.
- **A "low level"** exercise stress test: is used for patients with low and intermediate-risk unstable angina.

These "low level" exercise stress tests are limited either by:

workload 5-7 METs (i.e., 5-7 times the resting metabolic rate)
or heart rate < 120 beats/minute or less than 65% of predicted maximum heart rate.

These "low level" exercise stress tests are used to determine whether ischemia is present at levels of exercise likely to be encountered in ordinary daily activities or not. These tests are designed to increase safety in those patients with unstable angina.

Results:

It has a **sensitivity of 65-80%** and **specificity of 90%**. **A normal negative test** does not necessarily exclude coronary artery disease. It may be associated with an extremely low likelihood of a severe coronary artery disease such as 3-vessel or left main coronary disease.

A positive test of a "low level" exercise indicates **severe diseases** such as multi-vessel disease and is associated with a significantly increased risk of perioperative complications as myocardial infarction and death. The positive test is indicated by one of the following findings:

- > 1-2 mm horizontal or down sloping ST-segment depression.
- Persistence of ST depression after exercise for 5 min or longer.
- Sustained decrease in systolic blood pressure > 10 mm Hg for 10 min or longer after exercise.
- Failure to reach a maximum heart rate of > 70 % of the predicted.
- Frequent or complex ventricular dysrhythmias at a low heart rate.

Contraindications:

- Severe aortic stenosis.
- Severe hypertension.

- Acute myocarditis.
- Uncontrolled heart failure.
- Infective endocarditis.

N.B.: Recently Cardio-Pulmonary Exercise Testing "CPET": is used in some centers instead of the usual exercise ECG test with more predictive values of morbidity and mortality. It is discussed in more details at the end of this chapter.

4. Plain Chest X-ray: to exclude cardiomegaly, pulmonary vascular congestion, or pleural effusions.

5. Cardiac Enzymes:

	Onset	Peak	Duration
Creatine kinase myocardial bound "CK-MB" isoenzyme	3 hours	12 hours	36 hours
Lactate dehydrogenase (LDH) type 1	2 days	6 days	12 days
Cardiac troponin "I"	4 hours		7-10 days
Cardiac troponin "T"	4 hours		10-14 days

Both troponin "I" and "T" are more sensitive. Troponin "I" has a sensitivity of 100% and a specificity of 91%. They are normally 0.2 – 0.6 ng/mL. CK-MB has a sensitivity of 60% and a specificity of 94%.

The cardiac enzymes are released due to tissue necrosis in case of infarction (STEMI or non-STEMI).

N.B.: In unstable angina, CK-MB is not elevated, but troponin I and T may be elevated indicating the presence of micro-infarction.

N.B.: **CD 40 ligand** is increased due to platelet-monocyte aggregation as a thrombus is being formed; therefore, CD 40 ligand is used as a marker that indicates that ischemia will occur i.e., it increases even before troponin release and tissue necrosis.

6. Nuclear Stress Imaging (Scintigraphy) (Myocardial Perfusion Scans):

- It assesses regional blood flow and so can detect myocardial viability. It has a poor image resolution.
- A Tracer e.g., **thallium-201 or technetium-99m sesitamibi** is injected intravenously and then can be detected over the myocardium by single-photon emission computed tomography techniques.
- It is performed early within 3-4 hours after stress, late within 8-72 hours after stress, and at rest to detect rest-redistribution.
- Presence of a cold spot (i.e., does not take thallium) during stress only (and not during the resting status) indicates ischemia, but a constant cold spot (during rest or stress) indicates infarction as stress increases uptake of the tracers in normal cardiac tissues, but not in areas with obstructed coronary flow (figure 13-15 and 13-16).

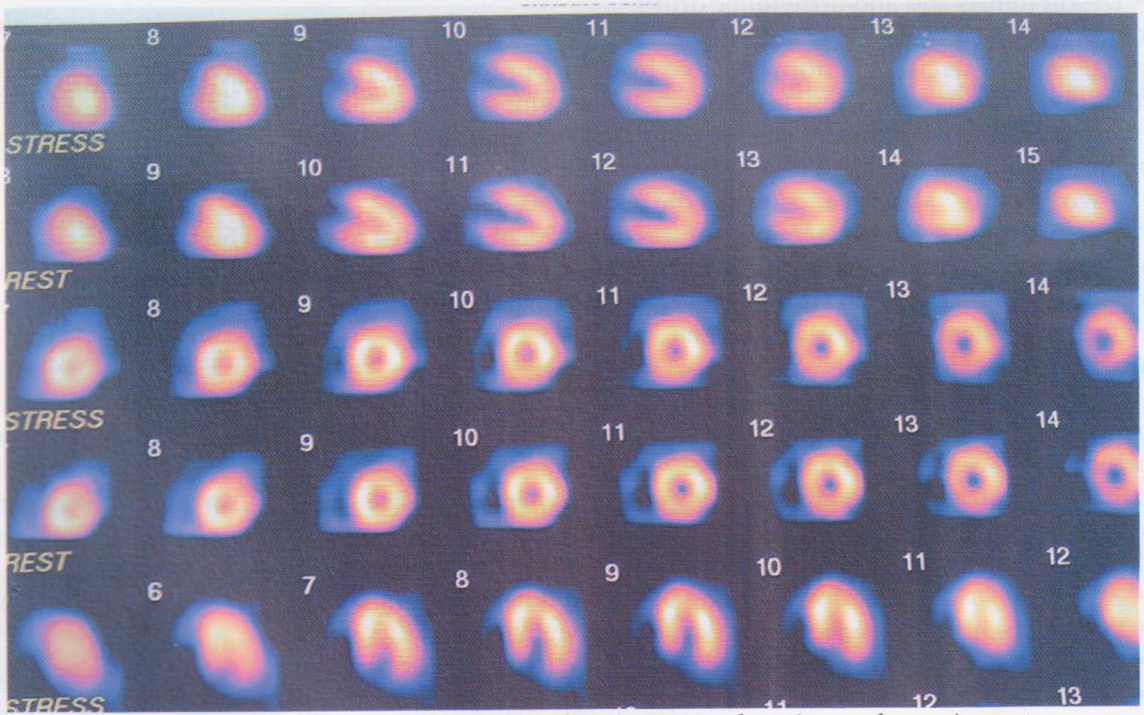


Figure 13-15: Nuclear stress imaging showing normal resting and exercise test

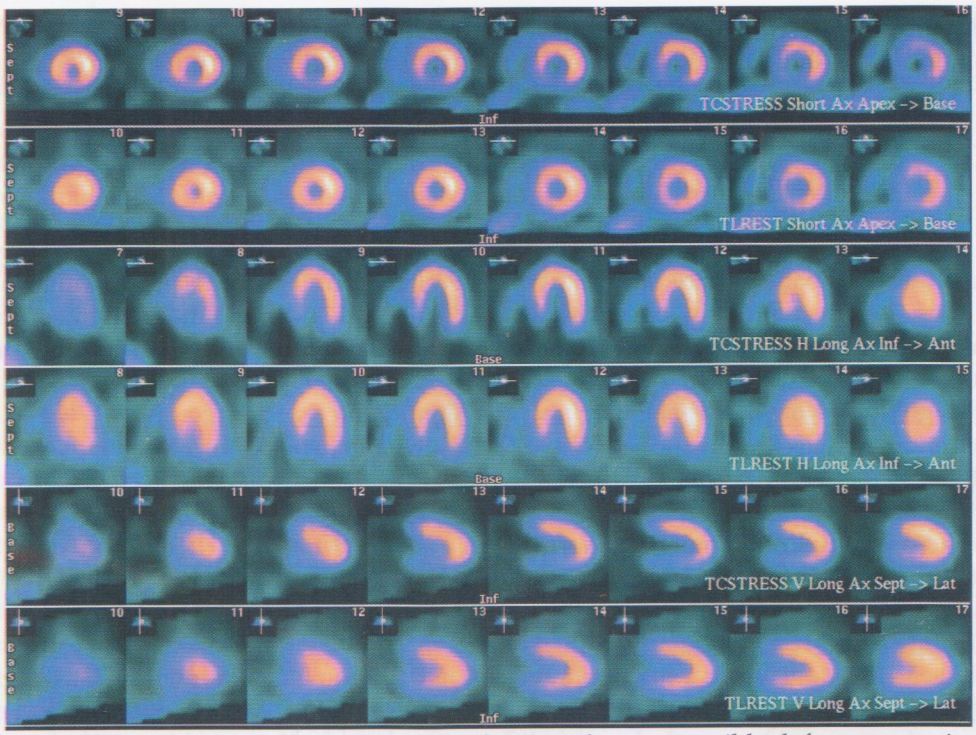


Figure 13-16: Nuclear stress imaging showing a moderate to large reversible defect present in the inferior and inferoseptal walls indicating ischemia in the distribution of the right coronary artery. The defect is completely reversible indicating myocardial viability.

N.B.: Stress can be induced either by:

- exercise,

or • pharmacologically: which is indicated in:

  - Patients who are intolerant to exercise e.g., peripheral vascular disease or musculoskeletal diseases.
  - Aortic aneurysm as exercise may cause its rupture.

The drugs used are either:

a- Drugs producing coronary vasodilatation to produce a hyperemic response similar to exercise (i.e., they mimic the coronary vasodilator response, but not the heart rate response associated with exercise). They include: either: ▫ Adenosine: that is a direct coronary vasodilator.

▫ Dipyridamole: that inhibits adenosine reuptake thus it increases its level leading to coronary vasodilatation. It may cause steal phenomenon.

b- Drugs increasing myocardial O_2 demand (i.e., they increase the heart rate). They include:

- dobutamine infusion (the most common agent used),
- isoproterenol or atropine.

Temporary pacemaker insertion can be used to increase the heart rate.

After cardiac stress, thallium imaging, echocardiography, or radionuclide angiography can be performed.

7. Radionuclide Angiography:

It has a 90% specificity and sensitivity.

It detects the ejection fraction and any new abnormal wall motion by using technetium pyrophosphate.

8. Two-Dimensional Echocardiography (Trans-Thoracic or Trans-Esophageal):

Trans-esophageal echocardiography gives better image quality then the trans-thoracic approach. It detects abnormal wall motion abnormalities and evaluates global and regional cardiac function. It is more sensitive than ECG and pulmonary artery catheterization.

Stress echocardiography can be done after dobutamine, atropine or dipyridamole injection as above.

9. Coronary Angiography and Cardiac Catheterization:

• It is the **gold standard** for evaluation of coronary artery diseases. Much information may be obtained from cardiac catheterization.

▫ A radiopaque contrast dye can be injected directly into the coronary arteries to define the anatomy of the coronary circulation and the degree of patency or sites of stenosis and obstruction.

- A radiopaque contrast material can be injected into the aorta or the ventricles to assess incompetence of valves and the efficacy of ventricular contraction (ejection fraction) and wall motion.
- Dysfunction and failure of the heart can be identified by pressure monitoring across the stenosed valves.
- Oximetry of blood at different sites indicates if shunts are present.
- Cardiac output may be measured.

• It is done to assess the patient's benefit before: percutaneous trans-luminal coronary angioplasty, or coronary artery bypass grafting surgery (CABG).

Percutaneous trans-luminal coronary angioplasty is useful in discrete, concentric, proximal, non-calcified vessels and those less then 5 mm in length, but CABG surgery is indicated in diseased coronary arteries with a high-grade proximal stenosis and those of reasonable size and those that are free of significant distal plaques.

Indicators of Significant Ventricular Dysfunction (Bad Ventricular Function):

- Left ventricular ejection fraction < 50% (0.5). It is the most important.
- Left ventricular end-diastolic pressure > 18 mm Hg.
- Cardiac index < 2 - 2.2 L/min/m^2.
- Marked or multiple wall motion abnormalities.
- Evidence of congestive heart failure.

Other Tests and Investigations not Routinely Performed:

1- Electron Beam Computed Tomography (CT scan):

It is a highly sensitive test, but is not specific and is not recommended routinely. It detects coronary artery calcifications because calcium forms deposits in atherosclerotic vessels. It also assesses the heart, great vessels, and associated lung pathology (to differentiate between lung and heart diseases).

Spiral CT (CT angiogram) with a contrast material can assess pulmonary artery thrombosis.

2- Magnetic Resonant Imaging (MRI):

It provides greater image clarity and can delineate the proximal portions of the coronary arterial circulation, but also not recommended routinely.

3- Positron Emission Tomography:

It assesses: • regional myocardial blood flow noninvasively, and • regional metabolic activity independent of the flow.

It can be used to delineate the extent of coronary artery disease and myocardial viability.

[^{18}F] Fluoro-deoxy-glucose (FDG) Imaging is an example of positron emission tomography.

It is a recent test where it is used as a marker for regional exogenous glucose utilization in hypoperfused regions. FDG is a glucose analogue that undergoes the same transport and phosphorylation of glucose, but does not enter glycolysis or glycogen synthesis.

Increase FDG uptake in regions with reduced perfusion is called FDG-blood flow mismatch indicating the presence of viable myocardium with reduced regional blood flow; a condition known as hibernation (see later). It is expensive and not readily available.

N.B.: Imaging Studies for Ischemic Heart Diseases include:

- Chest x-ray.
- Nuclear stress imaging (scintigraphy) (myocardial perfusion scans)
- Radionuclide angiography.
- Two-dimensional echocardiography (trans-thoracic or trans-esophageal).
- Coronary angiography and cardiac catheterization.
- Electron beam computed tomography (CT scan).
- Magnetic resonant imaging (MRI):
- Positron emission tomography and [^{18}F] Fluoro-deoxy-glucose (FDG) imaging

8. Premedications:

Premedications are the same as hypertension management regarding sedation and glycopyrrolate.

Intraoperative Management:

Aim: To maintain a favorable myocardial O_2 supply-demand balance. This is achieved by:

- Maintaining normal heart rate as increased heart rate (especially > 110/min) decreases diastolic coronary perfusion time.

- Maintaining normotension or slight hypotension as increased arterial blood pressure increases the afterload and contractility; this increases O_2 consumption. Diastolic blood pressure should be kept at ≥ 60 mm Hg to maintain coronary perfusion pressure.
- Maintaining adequate hemoglobin (Hb) concentration > 9-10 g/dL.
- Maintaining adequate arterial O_2 tension > 60 mm Hg.
- Maintaining normocapnia because hypercapnia causes dysrhythmias while hypocapnia causes peripheral and coronary vasoconstriction with shift of the O_2-Hb dissociation curve to the left.

Monitoring, Choice of Anesthesia, Recovery, and Extubation:

are the same principles that are discussed with hypertension.

Postoperative Management:

The aim of management is the same as those for intraoperative management. **Close monitoring** of patients to avoid postoperative myocardial ischemia is essential. Postoperative myocardial ischemia occurs most commonly in the **1st 3 days postoperatively** due to:

- Decreased O_2 supplementation.
- Starting movement of the patient.
- Decreased analgesia given to patients.
- The hypercoagulable response of surgery (although not proved clinically) due to increased platelet function and number, decreased fibrinolysis, decreased natural anticoagulants (protein C and anti-thrombin III) and increased procoagulants as fibrinogen, factor VIII and VW factor.
- Unintentional hypothermia that predisposes to shivering and increased O_2 need.
- Presence of anemia.

Therefore, prophylactic measures should be performed which include:

1. ECG and other investigations such as echocardiography that may be repeated every 8-12 hours the night of the surgery and then every day for 3 days as myocardial ischemia is usually silent postoperatively due to the analgesia received.
2. O_2 supplementation should be continued.
3. Proper treatment of postoperative pain is essential e.g.,
   - NSAIDs (analgesic + anti-platelet).
   - Epidural analgesia (it decreases pain, preload and afterload, and coagulation)
     Thoracic epidural causes coronary vasodilatation.
   - α_2 agonists as clonidine.
   - High dose sufentanil 1 µg/kg/hour + overnight controlled ventilation.
4. Proper treatment of postoperative hypothermia and shivering by warming the patient and by meperidine 20-30 mg i.v. with proper oxygenation.
5. Proper detection and treatment of postoperative pulmonary congestion by chest X- ray.
6. Proper treatment of anemia.
7- Perioperative continuation of beta-blockers if they were used.

If ischemia is detected, manage it "as above", and preferably in consultation with a cardiologist.

Q: What is the monitoring of myocardial ischemia in the perioperative period?
A: Discuss: • Definition and pathophysiology of myocardial ischemia.
• Preoperative, intraoperative and postoperative management.
Q: What is the postoperative management of myocardial infarction?
A: Discuss: • Definition and pathophysiology of myocardial ischemia.
• Preoperative, intraoperative and postoperative management.

Myocardial Stunning and Hibernation

There are 3 outcomes after myocardial ischemia (i.e., depressed flow and depressed function) which are:

1- Myocardial stunning.
2- Myocardial hibernation.
3- Myocardial infarction. It is irreversible with severe lethal cellular injury, both the flow and function are depressed (i.e., flow-function matching).

N.B.: Reperfusion injury is discussed in details in chapter "Cardiac Surgery".

Differences between These Conditions:

	Normal	Ischemia	Stunning	Hibernation	Infarction
Function	Normal	Lost	Lost	Lost	Lost
Coronary flow	Normal	Decreased	Normal	Chronic, but not severe decrease	Decreased
Hypoxia	Absent	Present	Absent	Absent	Present
Cell viability	Viable	Viable	Viable	Viable	Not viable

Myocardial Stunning

It was first described by Heyndrickx et al, in 1975.

Definition:

It is **a transient fully reversible** left ventricular dysfunction (detected by segmental wall motion abnormalities) that persists after reperfusion (**for hours to days**) i.e., delayed recovery with:

- Absence of irreversible damage (mild sub-lethal cellular injury).
- Restoration of normal or near-normal coronary flow (abnormal function with normal or near normal flow).

i.e., **flow-function mismatch or uncoupling.**

Mechanism:

Two theories are present.

1- Re-synthesis of adenosine tri-phosphate (ATP) is delayed because the precursors are washed out during the reperfusion period. This theory is not accepted nowadays due to:

- There is no correlation between the myocardial ATP level and recovery of contractility.
- The content of phospho-creatine in the stunned myocardium is normal or supernormal.
- The stunned myocardium responds to inotropic stimuli without a further decrease in ATP.

All these indicate that energy production is not impaired.

2- There are **O_2 and Ca^{++} toxicity during reperfusion, O_2 free radicals** are produced in excess of the capacity of the defense mechanisms causing an oxidative stress, which in turn causes membrane damage of the sarcolemma or sarcoplasmic reticulum, altering Ca^{++} homeostasis, and causing impaired contraction.

This is the most accepted theory nowadays.

Myocardial Hibernation

It was first described by Rahimtoola in 1985.

Definition:

It is **a chronic transient fully or partially reversible** left ventricular dysfunction (detected by segmental wall motion abnormalities) that occurs after prolonged (not severe) myocardial hypoperfusion with viable myocardium (myocytes), but with reduced contractility.

It is partially or fully reversed to normal after either:

- Restoration of coronary flow (in cases of ischemic heart diseases).
- Reduction of O_2 demand (in cases of chronic left ventricular overload).

Both flow and function are reduced i.e., flow- function match or coupling).

Mechanism:

The exact mechanism is **unknown**. During prolonged hypoperfusion, there is reduced energy supply as there is:

- Increased free fatty acid metabolism to glucose.
- Increased glycolysis.

Both cause downregulation of the contractile performance. There are many theories which explain this downregulation of contractility.

1- A decrease in coronary perfusion pressure causes a decreased sarcomere length due to distension in the adjacent coronary microvasculature. This decreases the extent of the contraction by Frank Starling mechanism.

However a lot of evidence is against this theory.

2- A decrease in energy stores causes downregulation of contraction, but the net ATP and CP stores are not depleted during hibernation.

3- Most recently, ischemia-induced activation of ATP/ADP modulated K^+ channels cause downregulation of contraction.

N.B.: Hibernation is not a state of chronic ischemia, but it is a state of chronic hypoperfusion with aerobic metabolism i.e., the residual flow is able to deliver enough O_2 to meet the reduced rate of mitochondria oxidation (still aerobic metabolism), in contrast to ischemia, where O_2 delivery is not enough to meet the reduced rate of mitochondria oxidation causing anaerobic metabolism. Therefore, in hibernation, the myocardium does not produce lactate (in contrast to ischemia where lactate is a typical marker).

Investigations:

To detect stunning, hibernation or infarction. They are discussed above.

1- Positron emission tomography such as [^{18}F] Fluoro-deoxy-glucose (FDG).
2- Thallium myocardial imaging.
3- Echocardiography during low-dose dobutamine infusion.

Treatment:

Before treatment:

1- First, differentiate whether or not the dysfunctioning myocardium is viable (i.e., stunning or hibernation) or non-viable (i.e., infarction).

2- Second, differentiate whether it is normally perfused (i.e., stunning) or hypoperfused (i.e., hibernation).

Both (1) and (2) can be done by - Positron Emission Tomography.
- Thallium Myocardial Imaging.
- [^{18}F] Fluoro-deoxy-glucose (FDG).

3- Third, test the contractile reserve of the akinetic myocardium to confirm the viability by low-dose dobutamine echocardiography.

It is a reversible condition, so the treatment should be given only to the high risk group during stunning to:

- Prevent recurrence of stunning,

and - Prevent occurrence of ischemia.

Stunning occurs in:

1- Coronary artery disease patients with repeated episodes of ischemia which cause repeated stunning and lead to the occurrence of hibernation.

2- Reperfusion after Prinzmetal's angina (i.e., resolution of coronary artery spasm).

3- Reperfusion after acute myocardial infarction or unstable angina either by thrombolysis and/or coronary angioplasty.

4- Reperfusion after open heart surgery.

5- Reperfusion after cardiac transplantation.

The treatment includes:

1) Inotropic agents: such s dopamine, isoproterenol, epinephrine, hydralazine, and Ca^{++}.

They are only used in patients with stunning without ischemia as inotropes can be harmful if there is ischemia.

2) Ca^{++} antagonist: It has 2 actions.

• A hemodynamic action:

It decreases the afterload, preload, heart rate, and increases regional blood flow.

Dihydro-pyridines cause reflex sympathetic stimulation which indirectly stimulates the stunned myocardium.

A direct protective action of the drug might be present.

3) Anti-oxidants: such as

• N-2-Mercapto-propionyl-glycine.

• Desferrioxamine.

They are O_2 free radical scavengers (they have no hemodynamic action). They should be given just before reperfusion.

Treatment is mainly by revascularization either by:

• open heart surgery,

or • angioplasty.

N.B.: Revascularization of patients with end-stage ischemic cardiomyopathy and congestive heart failure may be considered an alternative to cardiac transplantation, as it improves mortality and morbidity, provided that many areas of the heart are viable (hibernating).

Valvular Heart Diseases

Preoperative Management (and Assessment)

Preoperative assessment by history, examination, and investigations is important to detect:

1- The Severity of the Valve Lesion:

The severity of the valve lesion is mainly detected by history namely the exercise tolerance. The patients are classified by **New York Heart Association (NYHA) Classification** as follows:

It is determined by symptoms (mainly dyspnea and fatigue).

Class I: No symptoms i.e., no limitation of physical activity.

Class II: Symptoms with ordinary activity i.e., slight limitation of physical activity.

Class III: Symptoms with less than ordinary activity i.e., marked limitation of physical activity.

Class IV: Symptoms at rest i.e., the patient can not do any physical activity without discomfort.

Examination and investigations are used to detect the severity (see later).

2- The Associated Diseases and Complications:

Such as hypertension, myocardial ischemia, and congestive heart failure.

3- Preoperative Drugs Taken:

The Usual Medications:

• β-blockers, calcium channel blockers, and digitalis are used to control heart rate.

• Angiotensin-converting enzyme inhibitors (ACEIs) and vasodilators are used to detect blood pressure and afterload.

• Diuretics, inotropes and vasodilators are used to control heart failure.

• Antiarrhythmics are used to control arrhythmias.

These drugs except diuretics and ACEIs should be **continued until the day of surgery**. The **side effects** of these drugs should be considered.

Anticoagulant Therapy: is given to decrease the risk of thrombosis.

a. **For most patients**:

Anticoagulant therapy (e.g., **warfarin**) can be **stopped 2-3 days before** surgery and **restarted 2-3 days after** surgery.

b. **For high risk patients** such as those with:

- previous history of embolism,
- atrial fibrillation,
- a thrombus,
- prosthetic valves especially in the mitral or tricuspid position.
  - Mechanical valves such as caged-ball valves (carry the greatest risk) or tilting disc valves (carry the intermediate risk).
  - Bio-prosthetic valves: heterografts such as porcine or bovine tissue aortic valves, or homografts which are preserved human aortic valves.

The bio-prosthetic valves carry the lowest risk.

Stop warfarin 3-5 days before surgery (according to the type of surgery) and do **prothrombin time** (PT) daily (it should **not be > 1.5 times the control** at the time of surgery). If it is prolonged, give vitamin K or fresh frozen plasma (FFP) (in emergency surgery).

I.v. unfractionated heparin or **subcutaneous low molecular weight heparin** is given after discontinuation of warfarin and continued **until the day before the day of surgery**.

After minor surgery, **warfarin** can be **restarted** on the 1st day postoperatively with PT control.

After major surgery, **heparin infusion** can be started **12-24 hours postoperatively** with thrombin control and can be continued until warfarin therapy is restarted once surgical hemostasis is felt to be adequate. Replacement by heparin allows rapid reversal of heparin by protamine, besides heparin is short acting.

More details about perioperative management of patients with anticoagulants is discussed in chapter of "Blood Diseases".

Antibiotic Prophylaxis against Infective Endocarditis:

The causative organisms are - the viridans group of streptococci (mainly),
- Gram-negative organisms
- enterococci faecalis
- staphylococci; especially after cardiac surgery or in i.v. drug abusers

or - coxiella burnetii.

Previously, the American Heart Association (AHA) was recommending a regimen for antibiotic prophylaxis against infective endocarditis. This regimen includes:

I. For dental, oral, nasal, pharyngeal, upper airway procedures or any incision and drainage.

A. Moderate risk (most other congenital heart diseases, acquired valvular dysfunction such as rheumatic heart diseases, hypertrophic cardiomyopathy, mitral valve prolapse with mitral regurgitation and/or thickened leaflets):

• Amoxicillin: adults 2 g (children 50 mg/kg) orally 1 hour before procedure.

For those unable to take oral medications, ampicillin: adults, 2 g (children, 50 mg/kg) i.m or i.v. 30 min before procedure.

B. Moderate risk with penicillin/amoxicillin/ampicillin allergy:

• Clindamycin: adults, 600 mg (children 20 mg/kg) orally, 1 hour before procedure or
• Cephalexin or Cefadroxil: adults 2 g (children, 50 mg/kg) orally, 1 hour before procedure or
• Azithromycin or Clarithromycin: adults: 500 mg (children, 15 mg/kg) orally 1 hour before procedure.

Patients unable to take oral medications:

• Clindamycin: the same doses above i.v. 30 min before procedure or,
• Cefazolin: adults, 1.0 g (children, 25 mg/kg) i.m. or i.v. within 30 min before procedure.

C. High risk: includes (prosthetic valve including bio-prosthetic valves, prior endocarditis, complex cyanotic congenital heart diseases such as single ventricle states, transposition of great vessels, tetralogy of Fallot, or surgically corrected systemic pulmonary shunts):

• Ampicillin: adults, 2 g (children, 50 mg/kg) plus gentamycin 1.5 mg/kg (up to 120 mg) for both adults and children i.v. or i.m. within 30 min before starting procedure,

then 6 hours after, ampicillin 1 g adults (children, 25 mg/kg) or amoxicillin adults 1 g (children, 25 mg/kg) orally.

D. High risk with penicillin allergy.

• Vancomycin: adults, 1 g (children, 20 mg/kg) i.v. infusion over 1-2 hour; complete infusion within 30 min of starting the procedure.

II. For genitourinary or gastrointestinal procedures.

A. Moderate risk:

• Amoxicillin or ampicillin: The same as moderate risk of group I.

B. Moderate risk with penicillin/amoxicillin/ampicillin allergy:

• Vancomycin: the same as the high risk with penicillin allergy of group I.

C. High risk:

• Ampicillin plus gentamycin: the same as high risk of group I.

D. High risk with penicillin allergy:

• Vancomycin (the same doses as above) plus gentamycin (the same doses as above).

These recommendations have changed and been updated because **recent researches** suggest that:

• Infective endocarditis is much more likely to result from frequent exposure to **bacteremia associated with daily activities** than from bacteremia associated with dental, gastrointestinal, or genitourinary tract procedures. For example, maintenance of good oral health and oral hygiene reduces bacteremia associated with normal daily activities (chewing, teeth brushing, flossing, use of toothpicks…etc.) and is more important than prophylactic antibiotics in reducing the risk of endocarditis.

• The risk of **antibiotic associated adverse effects** exceeds the benefits of endocarditis prophylaxis such as the emergence of antibiotic-resistant organisms.

• **Infective endocarditis prophylaxis should** not be directed to all individuals with dental, respiratory, gastrointestinal, genitourinary tract procedures or those with congenital heart diseases, but rather to **those individuals at highest risk of adverse outcomes if they develop endocarditis**. It appears that only a very small group of patients with heart diseases is likely to have the most severe forms and complications of endocarditis.

Recently updated recommendations by AHA include:

1- Antibiotic prophylaxis for endocarditis is recommended only for the following conditions:

- **Prosthetic cardiac valve** or prosthetic material used for cardiac valve repair.
- **Previous infective endocarditis**.
- **Congenital heart diseases**:
  - Unrepaired cyanotic congenital heart diseases, including palliative shunts and conduits.
  - Completely repaired congenital heart defects with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure (because endothelialization of prosthetic material occurs within 6 months after the procedure).
  - Repaired congenital heart diseases with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization).

It is no longer recommended for any forms of congenital heart diseases.

2- Antibiotic prophylaxis is recommended for **dental procedures** that involve manipulation of gingival tissues or the peri-apical regions of teeth or perforation of the oral mucosa.

3- Antibiotic prophylaxis is recommended for **invasive procedures** (i.e., those that involve incision or biopsy) **on the respiratory tract or infected skin, skin structures or musculoskeletal tissues**.

4- Antibiotic prophylaxis is **not recommended for genitorurinary or gastrointestinal tract procedures**.

The recent recommended antibiotic prophylaxis for a dental procedure:

For most patients: Oral: Amoxicillin.

Patients unable to take oral medications: ampicillin i.v. or i.m.

For patients allergic to penicillin/ampicillin:

Oral: Clindamycin, Cephalexin, Cefadroxil, Azithromycin, or Clarithromycin.

Patients unable to take oral medications: Clindamycin or Cefazolin.

The doses are the same as above.

4- Preoperative Premedications:

Decrease the dose of premedications in proportion to the severity of the ventricular impairment:

In good ventricular function, decrease anxiety.

In poor ventricular function as heart failure, omit premedications.

5- Preoperative Investigations:

1- ECG:

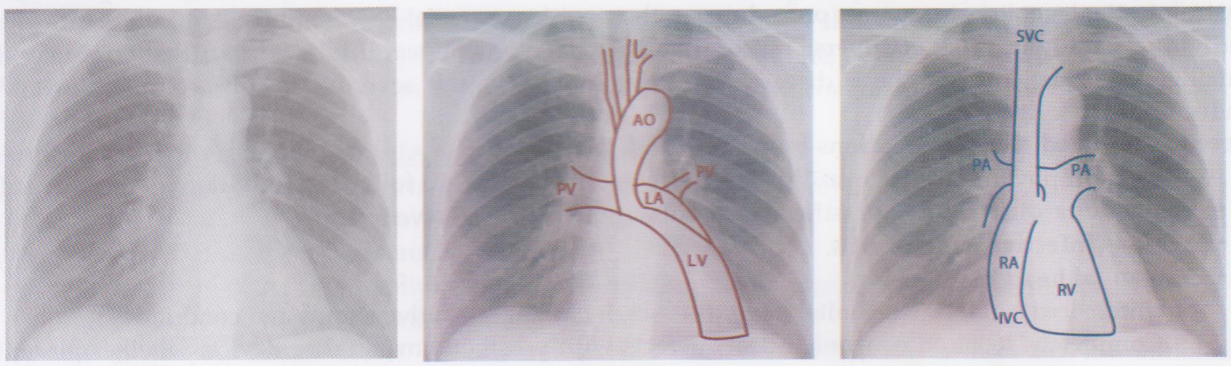
Value: to determine cardiac chamber enlargement, arrhythmias, ischemia…etc.
Left atrial hypertrophy: wide P (broad and bifid) (P mitrale), best in lead II.
Right atrial hypertrophy: tall peaked (P Pulmonale) P wave, best in Lead II.
Left ventricular hypertrophy: deep S in V_1, tall R in $V_{5, 6}$, aVL, aVF and left axis deviation.
Right ventricular hypertrophy: deep S in $V_{5,6}$, tall R in V_1 and right axis deviation.

2- Chest X-ray:

It can determine the following conditions:

- Cardiac enlargement: on postero-anterior chest radiographs, cardiomegaly can be noted if the heart size exceeds 50% of the internal width of the thoracic cage.
- Pulmonary congestion, and cardiogenic pulmonary edema: with central or peri-hilar infiltrates.
- Enlargement of pulmonary artery, left atrium, and left ventricle can be noted along the left heart border.
- Enlargement of right atrial and right ventricle can be noted along the right heart border.
- Valvular calcifications may be identified.
- Vascular markings in the peripheral lung fields are spare in the presence of significant pulmonary hypertension.

The following postero-anterior (PA) chest x-rays are normal x-rays with marks of the structures of the chest (figure 13-17).



AO Ascending aorta
LA Left atrium
PV Pulmonary vein
LV Left ventricle
SVC Superior vena cava
RV Right ventricle
PA Pulmonary artery
IVC Inferior vena cava
RA Right atrium

Figure 13-17: Normal PA chest x-ray

The following postero-anterior (PA) chest-x-rays are examples of different conditions associated in cardiovascular diseases (figure 13-18, 13-19, 13-20, 13-21, 13-22, 13-23, and 13-24).

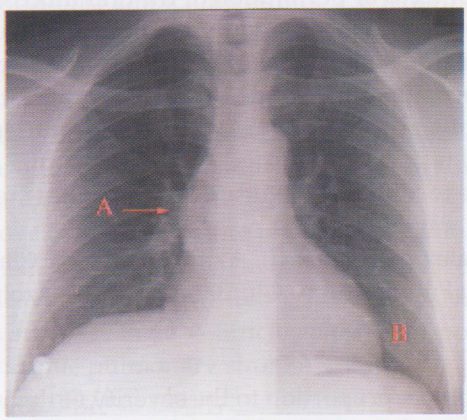


Figure 13-18: PA chest x-ray of a chronic hypertensive patient showing prominent ascending aorta (A), prominent left ventricular apex (B) without cardiomegaly due to left ventricular hypertrophy rather than left ventricular dilatation

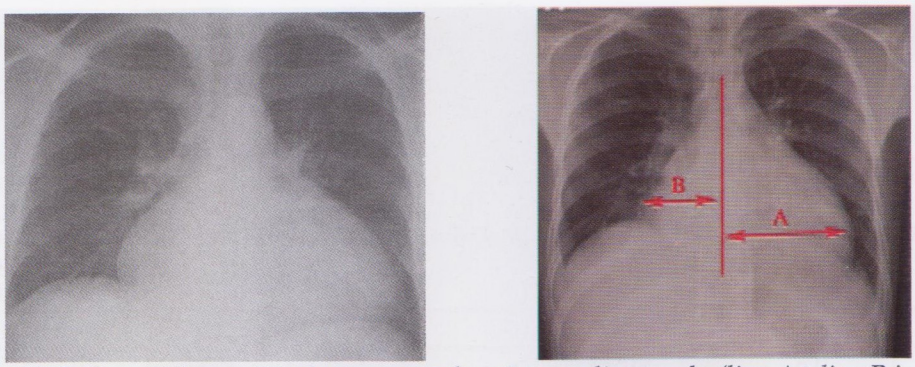


Figure 13-19: Two different PA chest x-rays showing cardiomegaly (line A+ line B is > 50% of the chest width) with left ventricular enlargement where the cardiac apex shows downward and left displacement (dilated cardiomyopathy)

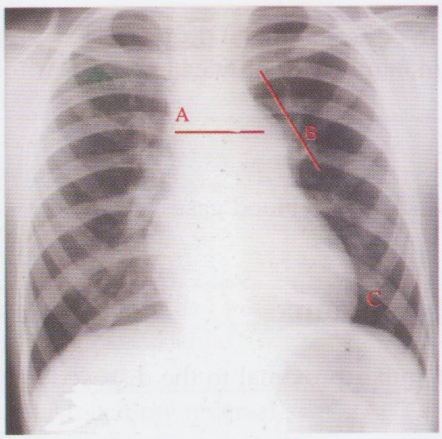


Figure 13-20: PA chest x-ray showing right ventricular enlargement with filling of the waist of the heart (A), straightening of the left border (B), and rounded apex (C)

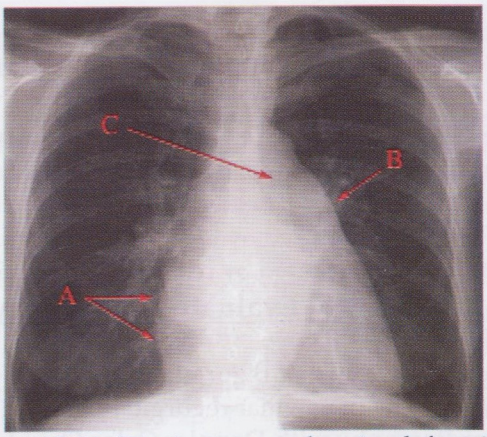


Figure 13-21: PA chest x-ray showing left atrial enlargement (due to mitral stenosis) with double density of the right atrium (A), straightening of left cardiac border due to left atrial appendage enlargement (B), and splaying of the carina with elevation of the left bronchus (C)

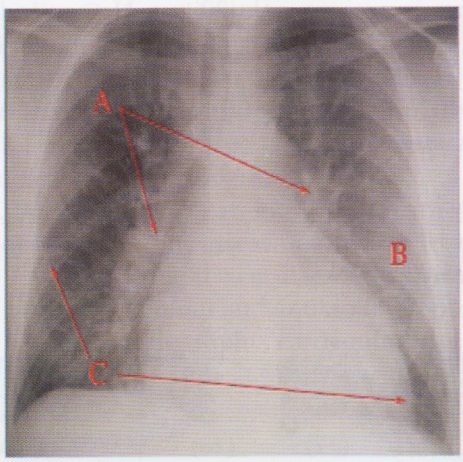


Figure 13-22: PA chest x-ray showing pulmonary edema and congestive heart failure with cardiomegaly, marked prominence of pulmonary vasculature (A), increased density in the alveolar spaces of the lung peripherally (B), small linear septal densities known as "Kerley B lines" (C)

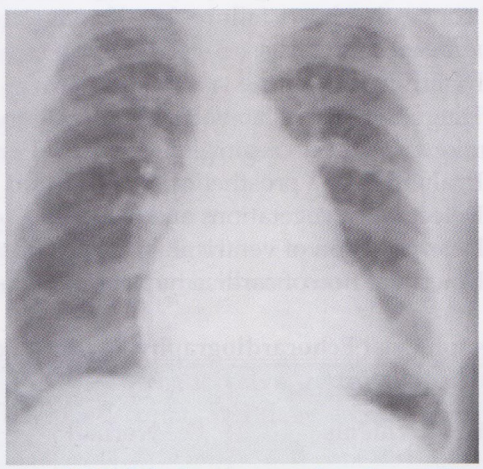


Figure 13-23: PA chest x-ray showing pulmonary congestion with left atrial appendage enlargement

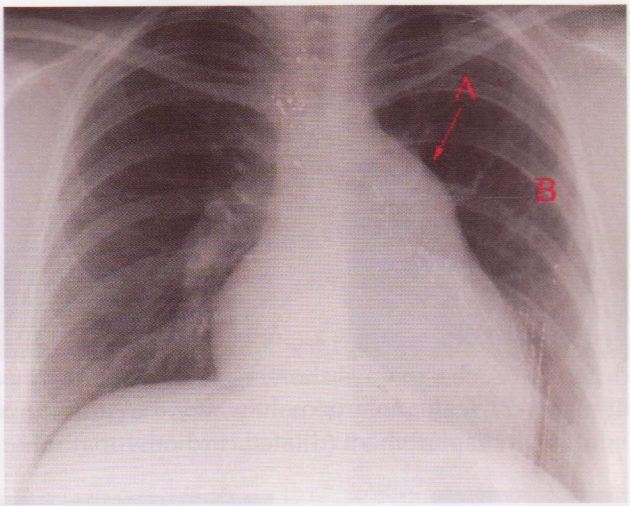


Figure 13-24: PA chest x-ray showing pulmonary hypertension with prominent pulmonary artery segment (A) and decreased pulmonary vascular markings (B)

3- Investigations for the Associated Complications:

- Cardiac ischemia investigations are discussed before.
- Pulmonary function is assessed by pulmonary function tests and arterial blood gases.
- Liver function is assessed by liver function tests.
- Renal function is assessed by renal function tests.

4- Investigations to Evaluate the Severity of the Valve Lesion:

a. Cardiography:

An angiographic dye that regurgitates back into the cardiac chamber proximal to the diseased valve can assess the severity of valvular regurgitation.

b. Echocardiography with Doppler Color Flow Imaging:

It allows:

- Determination of cardiac murmurs.
- Identification of hemodynamic abnormalities associated with physical findings.
- Identification of trans-valvular pressure gradient (also can be assessed by cardiac catheterization) especially in stenotic lesions (mitral stenosis and aortic stenosis). Both are considered to be severe when the trans-valvular pressure gradient is greater than 10 and 50 mm Hg respectively in absence of congestive heart failure, but if congestive heart failure is present, only 20 mm Hg can indicate severe aortic stenosis.
- Determination of the valve orifice area.
- Diagnosis of cardiac valve regurgitation by color flow Doppler. In mitral regurgitation, forward stroke volume and regurgitant stroke volume should be assessed.
- Evaluation of a prosthetic valve function.
- Detection of vegetations and thrombi.
- Determination of ventricular ejection fraction.
- Determination of cardiac hypertrophy and cavity dimensions.

Trans-Esophageal Echocardiography Severity Scale of Valvular Lesions:

Measurements	Normal	Severity Scales		
		Mild (+1)	Moderate (+2) (+3)	Severe (Critical) (+4)
A) Mitral stenosis (MS) Mitral valve area (cm^2)	4.0-6.0	1.5-2.5	1.0 - 1.5	< 1.0
Mean trans-valvular pressure gradient (mm Hg)	< 2	2.0-6.0	6.0 - 12.0	> 12
Pressure half time (msec)		100	200	> 300

B) Aortic stenosis (AS) Aortic valve area (cm^2)	2.5-3.5	1.2-2.0	0.8 - 1.1		< 0.8
Peak trans-valvular pressure gradient (mm Hg)	< 10	16-34	35 - 75		> 75
Mean trans-valvular pressure gradient (mm Hg)		< 20	20 - 50		> 50
C) Mitral regurgitation (MR) Jet length/left atrial length	0	< 1/3	1/3 - 2/3		> 2/3
Jet area/left atrial area	0	< 1/3	1/3 - 2/3		> 2/3
Jet area (cm^2)	0	< 3	3.0 - 6.0		> 6
Pulmonary vein Doppler S = systolic D = diastolic	S wave >> D wave	Blunting S wave	S<D	S<<D	Systolic reversal of flow
Regurgitant fraction	0	20-30	30 - 50		> 55
D) Aortic regurgitation (AR) Jet width/left ventricular outflow tract width	0	< 1/4	1/4-1/2	1/2-2/3	> 2/3
Jet length (pressure dependent)	0	To middle of anterior mitral leaflet	To tip of anterior mitral leaflet	To papillary muscle	Beyond papillary muscle
Regurgitant jet area as percent of left ventricular outflow tract area	0	4-24	25 - 59		> 60
Aortic diastolic flow reversal		None			Diastolic retrograde flow in the descending aorta

N.B.: Valve regurgitation = valve insufficiency

c. Cardiac Magnetic Resonance Imaging (Cardiac MRI).

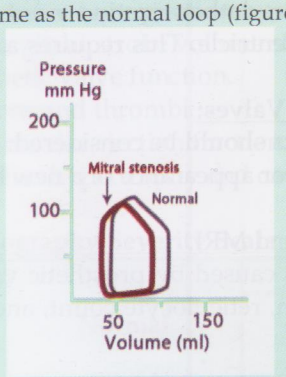
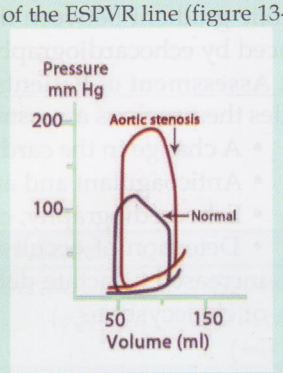
d. Cardiac Catheterization:

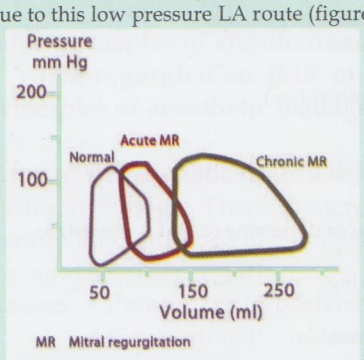
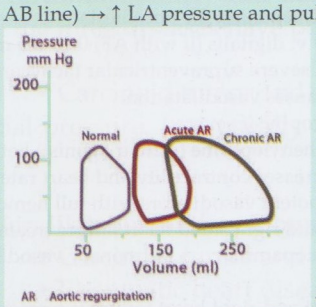
It gives an idea about severity of valve lesion, coronary artery diseases, and intracardiac shunts. It measures the pressure gradient across the valves in aortic stenosis, aortic regurgitation, mitral regurgitation and mitral stenosis, but in the latter, catheterization needs direct measurement of the diastolic gradient between the left atrium and left ventricle. This requires a trans-atrial puncture; so, it is replaced by echocardiography.

N.B.: Assessment of Patients with Prosthetic Heart Valves:

Besides the previous assessment; the following points should be considered:

- A change in the cardiac valve sound (clicks) or appearance of a new heart murmur.
- Anticoagulant and antibiotic prophylaxis.
- Echocardiography, cardiac catheterization, and MRI.
- Detection of occult intravascular hemolysis caused by prosthetic valve dysfunction as there are increased s. lactate dehydrogenase, s. bilirubin, reticulocyte count, and there is increased incidence of cholecystitis.

	Mitral Stenosis (MS)	Aortic Stenosis (AS)
Causes	1. Rheumatic fever (the commonest) due to fusion of the mitral valve leaflets during the healing process of acute rheumatic carditis. 2. Congenital. 3. Systemic Lupus Erythematosis or rheumatoid arthritis. 4. Carcinoid tumors and syndrome. 5. Left atrial myxoma or thrombus formation.	1. Rheumatic fever. 2. Congenital (usually bicuspid valve). 3. Degenerative senile calcification.
Patho - physiology • CO = cardiac output • SV = stroke volume • LAP = left atrial pressure • P++ = pulmonary hypertension • RVF = Right ventricular failure • RVD = Right ventricular dilatation. • LVF = Left ventricular failure • LVD =Left ventricular dilatation • PCWP =Pulmonary capillary wedge pressure • TR =Tricuspid regurgitation • PR =Pulmonary regurgitation • AF =Atrial fibrillation • CHF = Congestive heart failure • LVEDV = Left ventricular end diastolic volume • LVEDP = Left ventricular end-diastolic pressure • ↑= Increase or increased • ↓= Decrease or decreased • →= Causes or leads to	■ Pathological sequences: MS causes: a- ↑ LAP (and ↑ PAP and ↑ PCWP > 25 mm Hg) → • Acute → pulmonary edema especially with AF, sepsis, pain, and pregnancy. • Chronic → ↑ lymphatic drainage from the lung and thickening of the capillary basement membrane i.e., (irreversible pulmonary vascular resistance) → P++ without development of pulmonary edema. These events → RVD → RVF → TR and PR. b- ↓ ventricular filling (especially with AF) → low fixed cardiac output i.e., without a reserve to compensate for changes in heart rate or blood pressure. ■ Clinical picture and complications: • Pulmonary congestion. • AF present in 1/3 of severe MS with embolic manifestations. ■ Murmur: **Mid-diastolic rumbling** murmur with pre-systolic accentuation best heard at mitral area, axilla or apex. **Opening snap** in early diastole, caused by a vibration set in motion when the mobile but stenosed valve initially opens. It disappears if calcification occurs in the valve. ■ The amount of blood flow via MS depend on: 1. **CO**: is low, fixed, and heart rate dependent 2. **Heart rate: (diastolic time)** as ↑ heart rate → ↓ diastolic filling time →↓ CO ↓ heart rate with limited stroke volume due to the stenosed valve → ↓ CO 3. Atrial systole as **AF** → loss of atrial contractions → ↓ ventricular filling → ↓ CO 4. **Mitral valve orifice** (normally 4-6 cm^2) 1.5 - 2cm^2 → Asymptomatic 1-1.5 cm^2 → Dyspnea with mild to moderate exertion < 1 cm^2 → Dyspnea with minimal exertion and at rest (critical MS). ■ Pressure-volume loop (PV loop): The pressure-volume loop is **less useful** because the effects of MS occur proximal to the left ventricle. The pressure-volume loop of MS is nearly the same as the normal loop (figure13-25).  Figure 13-25	■ Pathological sequences: AS causes: a- ↑ LVP → LVD → LVF. b- ↓ Ventricular ejection → low fixed CO. ■ Clinical picture and complications: Orthostatic exertional dyspnea, syncope, angina, CHF, ventricular fibrillation and sudden death in 15-20%. ■ Murmur: **Harsh ejection systolic** murmur on the 2nd right intercostal space propagated to the carotid and apex. + Slowly rising low volume pulse with ↓ pulse + ↓ intensity of S_2 ■ The amount of blood flow via AS depend on: 1. **CO**: low, fixed, and heart rate dependent. 2. **Heart rate**: **(systolic time)** as ↑ heart rate → loss of timed atrial stroke → ↓ CO and ↓ time of coronary filling → angina ↓ HR → with limited stroke volume → ↓ CO. 3. Hypotension: → ↓ CO. 4. **Aortic valve orifice** (normally 2.5-3.5 cm^2) 0.9-2 cm^2 → asymptomatic 0.7-0.9 cm^2 → mild to moderate symptoms 0.5-0.7 cm^2 → critical AS. ■ Pressure-volume loop: PV loop is characterized by: • High **LV systolic pressure**. • Upward and counter clockwise rotation in the AB line which indicates ↓ **LV compliance** • The stroke volume and ejection fraction are well preserved, but the ejection phase (CD) occurs at a much higher pressure → ↑ **contractility** with counter clockwise rotation of the ESPVR line (figure 13-26).  Figure 13-26
Treatment	1. Medical: ↓ physical activity, ↓ salt intake, diuretics, digoxin, β blockers, and anticoagulants (caution with regional anesthesia). 2. Surgical: • Percutaneous trans-septal balloon valvuloplasty especially in severely ill pregnant patients • Open valvuloplasty. • Valve replacement	The same medical principles as mitral stenosis.

Mitral Regurgitation (MR)	Aortic Regurgitation (AR)	Tricuspid Regurgitation
a) Acute: • Ischemia or infarction • Infective endocarditis Both cause papillary muscle dysfunction or rupture of chordae tendinae. • Functional MR due to LVD b) Chronic: • Rheumatic fever (usually with MS) • Congenital • Systemic lupus, rheumatoid arthritis, or carcinoid tumor and syndrome.	a) Acute: • Infective endocarditis. • Trauma • Aortic dissection b) Chronic: • Rheumatic fever • Congenital (bicuspid valve) • Syphilis, cystic medial necrosis ± Marfan syndrome, use of anorexogenic drugs, ankylosing spondylitis, rheumatoid arthritis; they cause aortic dilatation and AR	1. LVF→ P^{++} → RVD (the most common). 2. Rheumatic fever 3. Infective endocarditis 4. Chest trauma 5. Ebstein's anomaly.
■ Pathological sequences: **During systole** → blood regurges to LA → • LAD → Acute → pulmonary congestion and edema Chronic → CHF • Low CO. **During diastole** → ↑ blood to LV → • Acute → no time for LVD or LVH • Chronic → ↑ LVEDV → maintaining normal CO, later → LVD and LVH So, LVF (with ↑ LVEDP + ↓ ejection fraction) → ↓ CO ■ Clinical picture and complications: • Acute: severe pulmonary edema and CHF. • Chronic: dyspnea on exertion, paroxysmal nocturnal dyspnea, and AF. ■ Murmur: **Pan-systolic** murmur on the apex propagating to the axilla. ■ The amount of blood regurgitant via MR depend on: 1. **Size of mitral valve orifice** 2. **Heart rate (systolic time).** 3. **LV – LA pressure gradient** during systole which is affected by LV outflow, ↓ systemic vascular resistance, ↑ LA pressure. Both decrease regurgitant volume. • **Severity**: If regurgitant fraction < 30% of SV → mild clinical picture. If regurgitant fraction 30-60 SV → moderate picture. If regurgitant fraction > 60% SV → Severe picture. ■ Pressure-volume loop (PV loop): • The diastolic PV relationship (line AB) is shifted to the right (as it is in AR) with a **marked increase in compliance.** • Isovolumetric phase (BC) is nearly absent as the LA serves as a low pressure / high compliance route for ejection due to the incompetent valve. • **Contractility is decreased** shown by a decrease in the slope of the ESPVR line (line through D). • Stroke volume and ejection fraction are maintained due to this low pressure LA route (figure 13-27).  Figure 13-27	■ Pathological sequences: **During systole** → ejection of ↑ amount of blood. **During diastole** → blood regurges to LV → • ↓ diastolic blood pressure. • Acute → no time for LVD. • Chronic → largest ↑ LVEDV of any heart disease → massive LVD called cor bovinum. Both acute and chronic → LVF (with ↑ LVEDP and ↓ ejection fraction) → Pulmonary congestion → - Acute : pulmonary edema - Chronic: CHF. ■ Clinical picture and complications: • Acute: severe pulmonary edema and CHF. • Chronic: dyspnea on exertion • AR causes the most dilated heart with decreased contractility resulting in heart failure. • Peripheral signs are present due to reflex peripheral VD → ↓ diastolic blood pressure → e.g., bounding pulse, wide pulse pressure, and decreased diastolic pressure. ■ Murmur: **Early diastolic blowing** murmur at the 2nd left intercostal space (2nd aortic area). ■ The amount of blood regurgitant via AR depends on: 1. **Size of aortic valve orifice.** 2. **Heart Rate (diastolic time)** as decreased heart rate → ↑ diastolic time → ↑ regurgitation. 3. **Diastolic pressure gradient** across the aortic valve (diastolic aortic pressure – LVEDP) So, ↑ diastolic blood pressure → ↑ regurgitation. • **Severity**: If regurgitant fraction < 30% of SV → mild picture. If regurgitant fraction 30-60% of SV → moderate picture. If regurgitant fraction > 60% of SV → severe picture. ■ Pressure-volume loop (PV loop) (figure 13-28): • Chronic: Line AB is shifted to the right with a **marked increase in compliance** (minimal change in LVEDP). Isovolumetric phase (DA) is absent • Acute: **LV compliance is unchanged** due to a rapid increase in LVEDP from volume overload (acute ↑ in AB line) → ↑ LA pressure and pulmonary congestion  Figure 13-28	TR → • Early: there is no ↑ in CVP or RAP because they are compliant, but later on → CHF→ **liver congestion** → hepatic dysfunction → **liver cirrhosis.** • Severe RVF with under loading of LV may → **right to left shunting** via an incompletely closed (or probe patent) foramen ovale → **marked hypoxemia;** therefore, meticulous de-airing of i.v. fluid systems is essential.
1. Medical: Diuretics, digoxin, ACEIs, β blockers especially carvedilol, and vasodilators. Inodilators such as dobutamine are useful due to their synergistic effects of positive inotropy and afterload reduction. 2. Surgical: Valve replacement.	The same medical principles as MR	Valve replacement

Anesthetic Management:

In stenotic lesions maintain **normotension, normal heart rate, and normal blood volume.**

<table>
<tr><th></th><th>Mitral Stenosis (MS)</th><th>Aortic Stenosis (AS)</th></tr>
<tr><td>Aim</td><td colspan="2">1. Heart Rate: maintain sinus rhythm optimally between 60-90/min
• Avoid AF as it impairs ventricular filling. It should be treated by immediate cardioversion.
• Avoid tachycardia as above.
• Avoid bradycardia as above.
2. Arterial blood pressure: maintain normal blood pressure (i.e., normal afterload)
• Avoid hypotension (and vasodilator drugs) because they produce severe hypotension, reduction of cardiac output and decrease coronary perfusion.
3. Fluid: maintain adequate blood volume (preload)
• Avoid hypovolemia as it produces severe hypotension.
• Avoid hypervolemia (i.e., increased central blood volume) as it increases pulmonary congestion. This can occur in over fluid transfusion, head down position, auto-transfusion during uterine contraction in labor.
4. Contractility: Myocardial support usually is not needed.
5. Avoid hypoxemia, hypercapnia, and acidosis because they cause pulmonary vasoconstriction which causes immediate right ventricular failure especially if with preexisting pulmonary hypertension.
N.B.: In patients with multiple valvular lesions, intraoperative management should be directed for the more severe valve pathology with keeping in mind that the stenotic lesions (especially AS) should have the highest priority in management.</td></tr>
<tr><td rowspan="2">Monitoring</td><td colspan="2">In all, the standard monitors + invasive blood pressure, central venous catheter, pulmonary artery catheter, and trans-esophageal echocardiography are used according to the severity of the condition.</td></tr>
<tr><td>Pulmonary capillary wedge pressure (PCWP): prominent a waves and a decreased y descent (PCWP represents trans-valvular pressure gradient and not LVEDP)</td><td>PCWP: prominent a wave.</td></tr>
<tr><td>Choice of Anesthesia:
a) Regional anesthesia</td><td colspan="2">The choice of anesthesia is according to the severity of the condition.

Regional anesthesia can be used in mild and moderate lesions with care to avoid hypotension.
Epidural is preferable to spinal anesthesia due to the more gradual onset of sympathetic block.</td></tr>
<tr><td>b) General anesthesia</td><td colspan="2">General anesthesia is generally more preferable than regional anesthesia.
<u>Induction:</u>
Slow smooth induction and decreased stress response to intubation is required by for example, opioids.
Etomidate is of choice, thiopentone in a small dose can be used, and ketamine should be avoided.
<u>Maintenance:</u>
If there is a good ventricular function, volatile based anesthesia is needed.
If there is a bad ventricular function, opioid based anesthesia is needed.
• Volatile agents: Halothane (if still present) is of choice because it decreases heart rate with the least vasodilatory effect. Isoflurane, sevoflurane, or desflurane can be used safely, but rapid increases in the concentration of desflurane may cause stimulation of sympathetic nervous system with accompanying tachycardia and pulmonary hypertension which are unwanted.
• N_2O: is used cautiously because it increases pulmonary vascular resistance resulting in pulmonary hypertension; therefore, it is avoided in patients with severe pulmonary hypertension.
• Muscle relaxants: Vecuronium or cis-atracurium is of choice.
Atracurium may cause histamine release with tachycardia and hypotension; so, may be avoided.
Pancuronium should be avoided as it increases heart rate.
The reverse is better with glycopyrrolate (than atropine).
• Intraoperative fluids: should be carefully estimated and replaced to avoid pulmonary edema.
• Patient position: Avoid head down position as it increases central blood volume.
• Intraoperative complications:
1. Tachycardia: treated by - Deepening the anesthesia - Opioid (except meperidine)
- i.v Esmolol - i.v. digitalis (if with AF) 0.25-0.5 mg over 10 min
- Cardioversion (in case of severe supraventricular tachycardia).
N.B. Avoid verapamil as it causes vasodilatation.
2. Bradycardia treated by atropine if severe.
3. Hypotension treated by phenylephrine (pure α agonist) better than ephedrine or dopamine (α and β agonist) as both have β action which increases contractility and heart rate).
4. Hypertension treated by potent vasodilators with full hemodynamic monitoring.
5. Pulmonary hypertension and right sided heart failure treated by:
- inotropic support e.g., dopamine - pulmonary vasodilators e.g., nitroprusside.
<u>Postoperative management:</u>
The risk of pulmonary edema and right heart failure is increased due to sympathetic stimulation caused by pain, hypoventilation (with respiratory acidosis) and hypoxemia. The latter causes pulmonary vasoconstriction; therefore, careful monitoring and O_2 supply are essential.
N.B.: In AS only: If cardiac arrest occurs, external cardiac massage is ineffective because it is difficult to create an adequate stroke volume across a stenotic valve; so, a defibrillator should always be available if anesthesia is given.</td></tr>
</table>

In incompetent valve lesions maintain **slight hypotension, slight tachycardia, and slight hypovolemia.**

Mitral Regurgitation (MR)	Aortic Regurgitation (AR)	Tricuspid Regurgitation (TR)
1. **Heart rate:** Maintain heart rate optimally **between 80-100/min** (except if with MS or AS). • Avoid tachycardia as it may produces ischemia. • Avoid bradycardia as it increases regurgitant volume. 2. **Arterial blood pressure:** Maintain **slight hypotension** (vasodilators are useful) • Avoid hypertension as it increases regurgitant volume. 3. **Fluid**: should be maintained (usually slight hypovolemia is beneficial). • Avoid hypervolemia as it causes more left ventricular dilatation resulting in decreased left ventricular contractility. • Avoid severe hypovolemia as it decreases ventricular filling volume resulting in decreased cardiac output. 4. **Contractility**: Myocardial support may be **needed**. • Avoid drug induced decreased contractility. 5. **Avoid hypoxemia, hypercapnia, and acidosis.**		• Avoid hypovolemia • Avoid positive end-expiratory pressure (PEEP) and high mean airway pressure during mechanical ventilation because they decrease venous return and increase right ventricular afterload. • **Avoid hypoxemia, hypercapnia, and acidosis.** • Avoid factors that increase pulmonary blood pressure such as N_2O.
In all, the standard monitors + invasive blood pressure, central venous catheter, pulmonary artery catheter, and trans-esophageal echocardiography are used according to the severity of the condition.		
PCWP: **large CV waves and rapid y descent**. The height of the CV wave is inversely related to atrial and pulmonary vascular compliance, but directly proportional to pulmonary blood flow and the regurgitation volume i.e., severity.	Arterial pulse: • Very wide pulse pressure. • **Bisferiens pulse** due to rapid ejection of a large stroke volume. PCWP: **large CV waves and rapid y descent** (suggests secondary MR due to left ventricular dilatation).	Central venous pressure increases in right ventricular failure. PCWP: **Large CV wave.**
The choice of anesthesia is according to the severity of the condition. Generally, both spinal and epidural blocks are well tolerated, if the patient has good ventricular function as long as there is no coagulopathy (especially in TR due to the affected liver function).		
Induction: Thiopentone, propofol, and ketamine can be used. **Maintenance:** If there is a good ventricular function, volatile based especially **isoflurane** can be used because it produces vasodilatation and slightly increased heart rate. If there is a bad ventricular function, opioid based anesthesia is used. • N_2O: is used cautiously because it increases pulmonary vascular resistance, and if used with opioids, severe myocardial depression occurs. • Muscle relaxants: Pancuronium is of choice because it produces slight tachycardia. Other agents without cardiac effects can be used safely. • **Intraoperative complications:** 1. **Bradycardia** treated by i.v. atropine 2. **Hypotension** treated by: ephedrine (with α and β agonist action) is better than phenylephrine (pure α agonist), but avoid large doses of vasopressors because they increase systemic vascular resistance, resulting in increased regurgitant volume. 3. **Hypertension** treated by: vasodilators with hemodynamic monitoring. 4. **Left ventricular failure** treated by inotropic support e.g., dopamine and systemic vasodilators e.g., nitroprusside. N.B.: Especially in **TR**, avoid i.v. infusion of **air bubbles** via tubing during fluid administration due to a possibility of right to left shunt that may cause a **paradoxical systemic embolism.**		

• **Valve stenosis (MS or AS), obstructive cardiomyopathy, and mitral valve prolapse** have nearly the same **principles of anesthetic management.**

• **Valve regurgitation (MR or AR), dilated cardiomyopathy, and heart failure** have nearly the **same principles of anesthetic management** because the three diseases have poor left ventricular function.

Tricuspid Stenosis:

Causes: • Rheumatic heart disease. • Carcinoid tumor and syndrome.

Pathophysiology: There is increased right atrial pressure. It is usually associated with TR which causes mainly the pathological changes.

Pulmonary Regurgitation:

Causes: • Pulmonary hypertension with annular dilatation of the pulmonary valve.
• Connective tissue diseases. • Carcinoid tumor and syndrome.
• Infective endocarditis. • Rheumatic heart diseases.

Pathophysiology: It is rarely symptomatic.

Pulmonary Stenosis:

Causes: • Congenital • Rheumatic heart diseases.
• Carcinoid tumor and syndrome. • Infective endocarditis.

Pathophysiology: There are usually syncope, angina, right ventricular hypertrophy, and right sided heart failure.

N.B.: Closed Mitral Valvotomy

Cardiac manipulation produces:

- a fall in blood pressure and arrhythmias; therefore, continuous monitoring is essential.
- dislodgment of clots; so, anesthesiologist is called to compress the carotid artery temporarily.

If the circulation after valvotomy does not improve, ask the surgeon not to manipulate the heart further until cardiac output has improved (the heart becomes now more responsive to inotropic drugs).

Mitral Valve Prolapse (Click Murmur Syndrome) (Floppy Valve Syndrome) (Barlow's Syndrome)

It is prolapse of one or both mitral leaflets into the left atrium during systole with or without mitral regurgitation.

Causes:

1- Familial: 5% of population especially females. It is **the most common valvular heart disease.**
2- Connective tissues disorders e.g., Marfan's syndrome, rheumatic carditis, myocarditis, thyrotoxicosis, and systemic lupus erythematosis.

Pathophysiology:

There are abnormalities of the mitral valve support structure i.e., there is myxomatous proliferation which causes thickening and redundancy of the mitral valve. This leads to prolapse of the mitral valve leaflets into the left atrium during left ventricular contraction. The posterior mitral leaflet is more commonly affected than the anterior leaflet.

Clinical Picture:

It may be asymptomatic, but there may be anxiety palpitations, orthostatic symptoms, dyspnea, and fatigue up to mitral regurgitation with mild to moderate heart failure.
It is accentuated by decreased ventricular volume (i.e., decreased preload).
Complications:

- Atrial tachyarrhythmias (paroxysmal supraventricular tachycardia is the most common and is responding to β-blockers) and ventricular arrhythmias (premature ventricular contractions are the most common). Prolonged QT interval is common.
- Infective endocarditis.
- Acute mitral regurgitation.
- Embolic phenomenon such as transient ischemic attacks (treated by aspirin and other antiplatelet agents) or left atrial thrombus (treated by warfarin).
- Heart block.
- Sudden death (rare).

Diagnosis:

- **Mid-systolic click at the apex** with/without **late apical systolic murmur.**
- **Echocardiography:** is the **best** for diagnosis as the mitral valve appears prolapsing 2 mm or more above the mitral annulus.

Anesthetic Management:

Aims: **Avoid decrease in ventricular size**; therefore,

- Avoid decreased preload (hypovolemia) because this causes greater systolic displacement of the leaflets into the left atrium.
- Avoid sympathetic stimulation by decreasing anxiety, using short acting β blockers to avoid tachycardia.
- Avoid decreased afterload (and systemic vascular resistance) by using vasopressors.
- Avoid anesthesia in head up or sitting position.

Choice of Anesthesia:

Regional Anesthesia: can be used safely as long as there is no hypotension, but it should be avoided because it may lead to hypotension (due to the associated decreased systemic vascular resistance).

General Anesthesia

The same anesthetic management is considered as mitral stenosis (or early mitral regurgitation). If frank mitral regurgitation occurs, the patient is managed as mitral regurgitation (see above).

Pulmonary Hypertension and Cor Pulmonale

Definition

Pulmonary Hypertension:

Mean pulmonary arterial pressure (PAP) is defined as > 25 mm Hg at rest,
and > 30 mm Hg with exercise.

Pulmonary vascular resistance is > 300 dyne.sec.cm^{-5}.

Severe pulmonary hypertension occurs when mean PAP is > 50 mm Hg

Or pulmonary vascular resistance is > 600 dyne.sec.cm^{-5}.

Cor Pulmonale:

It is pulmonary hypertension-induced impairment of the right ventricular structure (hypertrophy and dilatation) and function.

Causes

A- Primary (Idiopathic) Pulmonary Hypertension:

It is familial autosomal dominant inheritance present in 10% of cases.

Pathology:

There are increased anti-nuclear antibodies which indicate a collagen vascular disease associated with the vascularity of the pulmonary vessels. It is associated with other vasospastic conditions as Raynaud's phenomenon, prinzmetal angina, or migraine headache. It may be associated with advanced liver disease where vasospastic compounds bypass liver degeneration.

Clinical Picture: It occurs usually in females around 30 years of age.

It starts with exertional dyspnea, syncope, and angina. Death may occur within 15-20 years. Syncope occurs due to inability of stroke volume to be increased in front of pulmonary hypertension and sudden peripheral vasodilatation such as after exercise or a hot bath.

B- Secondary Pulmonary Hypertension:

$$PVR = \frac{PAP \quad LAP \times 80}{CO}$$

$$\text{Therefore, PAP (in mmHg)} = \frac{LAP + (CO \times PVR)}{80}$$

Where, PAP = pulmonary artery pressure in mm Hg.
LAP = left atrial pressure in mm Hg
CO = cardiac output in L/min
PVR = pulmonary vascular resistance in dyne.sec.cm^{-5}

From the above equation causes of pulmonary hypertension can be summarized as follows:

1- Causes of increased left atrial pressure:

- Left ventricular failure.
- Left sided valvular heart diseases (especially mitral stenosis and/or regurgitation).
- Left atrial myxoma.

2- Causes of increased cardiac output:

- Left to right shunt congenital heart diseases such as atrial septal defect or ventricular septal defect.

3- Causes of increased pulmonary vascular resistance:

- Pulmonary parenchymal diseases either:
  - obstructive: as chronic obstructive lung diseases (the most common cause) or cystic fibrosis.
  - restrictive: as sarcoidosis, tuberculosis, interstitial pulmonary fibrosis, or bronchiolitis obliterans.
- Hypoxia without pulmonary diseases such as hypoventilation or high altitude.
- Pulmonary arterial obstruction such as thromboembolism, or non-thrombotic pulmonary embolism as tumors, parasites (schistosomiasis), or foreign materials.
  Primary pulmonary hypertension belongs to this group.
- Chest wall diseases either:
  - Intrinsic such as kyphoscoliosis, thoracoplasty, or pectus deformity.
  - Extrinsic such as central nervous system disorders, poliomyelitis, or sleep apnea syndrome.

Pathophysiology

Normal Pulmonary Circulation:

- It accommodates nearly the whole flow of the systemic circulation ($\simeq$ 5 L/min at rest and up to 25 L/min during heavy exercise), while operating at 1/6 of the systemic pressure.

Pulmonary systolic blood pressure = 22 mm Hg, diastolic blood pressure = 10 mm Hg and mean blood pressure = 15 mm Hg.

The quantity of blood within the pulmonary circulation is ≃ 0.5- 1 L, while only 80 mL (≃ one cardiac stroke volume) are exposed to the gas-exchange surface of the pulmonary capillaries at any specific moment.

• Normally endogenous endothelial vasodilators (nitric oxide and prostacyclin) predominate although vasoconstrictors (endothelin and thromboxane) may modulate the pulmonary vascular resistance. Disruption of the endothelium and the endogenous vasodilators is associated with the development of pulmonary hypertension.

Factors Affecting Pulmonary Circulation:

1- Cardiac output: Increased cardiac output **decreases pulmonary vascular resistance** by:

- **Recruitment** (i.e., opening of the previously closed pulmonary vessels in the non-dependent lung).
- **Distension** (i.e., distension of the already opened pulmonary vessels in the dependent lung).

This relationship becomes less pronounced in disease states of the pulmonary circulation.

2- Airway pressure: increased airway pressure e.g., hyperinflation of the lung greatly **increases pulmonary vascular resistance** because it compresses the alveolar vessels.

3- Gravity: The lung is divided into 3 classic west zones. It is discussed in details in the chapter of "Respiratory Diseases". A 4th zone may be added which accounts for the increased interstitial pressure in the dependent zones which decreases perfusion. Ventilation is also greater in the dependent lung parts; so, in the abnormal lung area, there is ventilation/perfusion mismatching.

4- Hypoxia: Small areas of alveolar hypoxia cause diversion of blood flow and minimal changes in pulmonary vascular resistance. In this situation, hypoxic pulmonary vasoconstriction is a protective mechanism that improves ventilation/perfusion matching.

Large areas of hypoxia produce proportionally greater increases in pulmonary vascular resistance.

5- Acidosis (respiratory or metabolic): is a potent pulmonary vasoconstrictor while alkalosis is a potent pulmonary vasodilator.

6- Hypercarbia: induces pulmonary vasoconstriction.

7- Histamine releases: induces pulmonary vasoconstriction.

8- Atelectasis: can increase pulmonary vascular resistance via stimulation of hypoxic pulmonary vasoconstrictive reflex and mechanical compression; therefore, the lungs should be adequately expanded in patients with pulmonary hypertension.

9- Sympathetic stimulation, cold, and catecholamines: increase pulmonary vascular resistance.

10- α_1 agonists: increase pulmonary vascular resistance while β_2 agonists decrease it.

N.B.: While hypoxia, hypercarbia, acidosis, and histamine release produce pulmonary vasoconstriction, they produce systemic vasodilatation.

At least 50% reduction in the pulmonary vascular bed cross-sectional area must occur to increase the resting pulmonary artery pressure.

Right Ventricular Response:

Pulmonary hypertension leads to right ventricular dysfunction; the rate at which the right ventricular dysfunction (and congestive heart failure) develops, depends on the magnitude of the increased pressure in the pulmonary circulation and on the rapidity with which this increase occurs.

Acute increase in PAP e.g., pulmonary embolism causes right ventricular failure with a mean PAP as low as 30 mm Hg because increased PAP causes right ventricular distension. This increases the wall tension to a failure threshold **(La Place law is the wall tension = radius x intra-ventricular pressure).**

Chronic increase in PAP e.g., chronic obstructive pulmonary diseases (COPD) allows time for right ventricular hypertrophy (as a compensatory mechanism). This causes late right ventricular failure which usually occurs when the mean PAP exceeds 50 mm Hg. Acute right ventricular failure occurs when a patient with COPD is subjected to stress as infection, hypoxia, acidosis or fluid overload.

Effect of Right Ventricular Failure and Pulmonary Hypertension on Left Ventricular Function:

1- Increased pulmonary vascular resistance and right ventricular end-diastolic volume and pressure shift the interventricular septum towards the left ventricular cavity. Consequently, right ventricular failure may decrease left ventricular filling, increase pulmonary capillary wedge pressure, and decrease left ventricular output.

Echocardiography shows a dilated right ventricle and the septal curvature, which is normally to the right, is flattened or deviated to the left.

2- Right ventricular dilation also may cause an increase in intra-pericardial pressure that decreases left ventricular distensibility and compliance.

Therefore, right ventricular failure may significantly impair global cardiac performance and cardiac output; either due to right ventricular failure itself or by impacting left ventricular function.

Clinical Picture:

History: • Asymptomatic in many cases.
• Symptoms of congestive heart failure as cough, dyspnea, fatigue…etc.
• Symptoms of low cardiac output as exertional dyspnea and syncope…etc.
• Symptoms of the cause as chronic obstructive lung diseases.

Examination: The following pathology may be present:

• Congestive heart failure: as a prominent "a" wave, increased jugular venous pressure and pedal edema.
• Right ventricular hypertrophy as S2, S3, and S4 (gallop), parasternal heave along the left sternal border and possible diastolic pulmonary regurgitation murmur (Graham-Steel murmur) and systolic tricuspid regurgitation murmur.
• Pulmonary hypertension causes accentuated pulmonary component of S2.

Investigations:

1- **ECG:** may show • Right ventricular and right atrial hypertrophy with right axis deviation with/without strain pattern. Right bundle branch block may be present.
• Low voltages of QRS complexes in all leads (due to COPD).

2- **Plain chest x-ray:** may show:
• Right ventricular or right atrial enlargement.
• Parenchymal lung diseases.
• Pulmonary hypertension with:
- Decreased pulmonary vascular markings in lung periphery.
- Dilatation of the main pulmonary artery and central branches with possible calcification.

3- **Echocardiography:** may show right ventricular hypertrophy, pulmonary regurgitation, tricuspid regurgitation, and dilatation of the pulmonary artery. Trans-thoracic echocardiography is difficult to perform in patients with COPD because the hyper-inflated lungs impair transmission of ultrasound waves.

4- **Cardiac catheterization:** (right sided): is the gold standard.
• It differentiates right ventricular dysfunction secondary to left ventricular failure from that secondary to pulmonary hypertension where:
- In left ventricular failure, there is a normal diastolic PAP to PCWP gradient,
- while in pulmonary hypertension, there is increased diastolic PAP to PCWP gradient > 8 mm Hg.
• It measures PAP to evaluate or estimate the severity of pulmonary hypertension.
- Mild pulmonary hypertension: PAP increases to be > 20 mm Hg.
- Moderate pulmonary hypertension: PAP increases to be > 35 mm Hg.
- Severe pulmonary hypertension: PAP increases to be > 50 mmHg.
• It assesses the response to vasodilator therapy.

N.B.: Obliterative vascular diseases as primary pulmonary hypertension and recurrent thrombo-embolic disease are associated with the highest increase in mean PAP.

5- Pulmonary function tests and arterial blood gases: to detect restrictive or obstructive lung disease.

6- Pulmonary computed tomographic angiography may show vascular filling defects.

7- Sleep study especially for patients with sleep apnea syndrome.

Treatment

It is important to know if the patient has right ventricular failure, pulmonary hypertension, or both because the primary management differs according to the patient condition.

Patient Condition	Primary Treatment
Patients with pulmonary hypertension (without right ventricular failure)	• Vasodilator (i.v./inhaled) • ± volume optimization.
Patient with right ventricular failure (without pulmonary hypertension)	• Inotropes • ± volume optimization/diuretics. • + vasoconstrictor.
Patients with right ventricular failure (with pulmonary hypertension)	• Inotropes • + vasodilator (i.v./inhaler)

A) General Measures:

1- O_2 therapy:
• To maintain PaO_2 > 60 mm Hg or SaO_2 > 90%.

• Avoid excessive O_2 in COPD when the hypoxic drive is predominant.

Almitrine is an alternative to O_2 which improves ventilation/perfusion matching without affecting minute ventilation or the need to increase more O_2 administration by:

• stimulating the carotid body,

• producing vasoconstriction to the non-ventilated alveoli in COPD patients.

2- Anticoagulant (warfarin or antiplatelet): to prevent pulmonary emboli.

3- Antibiotics: The commonest organisms are Hemophilus or Pneumococci which are usually sensitive to ampicillin or cephalosporins.

4- Bronchodilators.

5- Correction of electrolyte imbalance.

B) Treatment of Right Ventricular Failure:

1- Inotropes:

• Dobutamine is better than dopamine because dobutamine lacks α action induced pulmonary vasoconstriction.

• Phosphodiesterase III inhibitors such as milrinone and amrinone have inotropic and nonspecific vasodilator actions; hence the term inodilator; therefore, they can be used for right ventricular failure and pulmonary hypertension.

• Digitalis: is given with care due to the increased risk of toxicity in presence of arterial hypoxemia, acidosis and electrolyte disturbances.

2- Volume optimization/diuretics:

• Avoid volume overload as it increases right ventricular end-diastolic volume.

• Diuretics: are given with care due to the following effects:

- Metabolic alkalosis which decreases ventilation by depressing the effectiveness of CO_2 as a respiratory stimulus.
- Increased blood viscosity which causes further increase in hematocrit.

3- Intra-aortic balloon pump.

C) Treatment of Pulmonary Hypertension:

Vasodilators are either specific or nonspecific. The specific (selective) drugs are more preferable.

a- Non-specific pulmonary vasodilators: produce systemic and pulmonary vasodilatation.

• Hydralazine	systemic	>>>	pulmonary
• Na Nitroprusside	systemic	>	pulmonary
• Nitroglycerin	systemic	>	pulmonary
• Nifedipine	systemic	>	pulmonary
• Isoprenaline	systemic	=	pulmonary

Disadvantages of the Nonspecific Agents: They produce

• Systemic hypotension which may decrease coronary perfusion leading to right ventricular ischemic failure.

• Attenuation of the localizing hypoxic pulmonary vasoconstrictive reflex; therefore, they may worsen ventilation/perfusion matching.

b- Specific (selective) pulmonary vasodilators:

• **Inhaled nitric oxide (NO)**: (10 ppm) is given by a specialized delivery system as a gas (all other inhaled drugs are given as a simple nebulized drug).

• **Prostaglandin I_2 (PGI_2) (prostacyclin)**:
Epoprostenol (*Flolan*): is used as i.v. infusion and has a very short half life.
Treprostinil (*Remodulin*): is used subcutaneously.
Iloprost (*Ventalis*): is used as inhalational form.

Generally, the inhaled drugs are more specific than the systemic drugs. Both inhaled NO and PGI_2 are equally effective, but NO is more expensive.

• **Phosphodiesterase inhibitors V: Sildenafil (*Viagra*)**: inhibits phosphodiesterase isoenzyme 5 which is highly concentrated in the lungs. It acts as NO and PGI_2 inducing agent. It is used either as oral or i.v. form.

• **Endothelin antagonists: as bosentan (*Traclear*)**: it is used as oral form.

N.B.: Endothelin receptors are two types:

Endothelin A receptors: cause pulmonary vasoconstriction and smooth muscle proliferation.

Endothelin B receptors: cause pulmonary vasodilatation via enhanced endothelin clearance and increased production of NO and PGI_2.

• **Other specific inhaled drugs** such as PGE_1, NO donors, sodium nitroprusside, nitroglycerine, phosphodiesterase inhibitors III as milrinone are under trials.

Advantages of the Selective Specific Agents (Especially the Inhaled Forms)

• They do not cause systemic hypotension.

• Especially in the inhaled forms, they produce pulmonary vasodilatation to the areas of the lungs where ventilation occurs resulting in improving ventilation/perfusion matching.

Anesthetic Management

Preoperative Management:

1- Preoperative evaluation: by history, examination and investigation as before.

2- Preoperative treatment of corpulmonale is discussed above.

Postpone elective surgery till properly treated to correct the reversible changes.

3- Preoperative correction of hematocrit (Hct):

• Chronic hypoxia causes secondary polycythemia (i.e., Hct > 60%) which in turn increases blood viscosity. This decreases O_2 carrying capacity and O_2 delivery to the tissues.

Therefore; decrease **Hct to 50-55%** by **euvolemic erythrophoresis or phlebotomy.**

• Value: - It decreases blood viscosity.
- It causes a small (2-3 mm Hg), but significant decrease in PAP.
- It causes a small (0.3 L/min/m^2), but significant increase in cardiac index.
- It causes little (18%), but significant increase in renal plasma flow.

• Precautions:
- Phlebotomies are most safely carried out in small quantities (300 mL) every 1-2 days with a recovery interval of 48 hours before an elective surgery.
- No further favorable shifts are documented by decreasing the Hct to be less than < 50%.

4- Premedications:

• Avoid sedatives and opioids as they might depress respiration. They are replaced by psychological support.

• Avoid anticholinergics due to - increased physiological dead space.
- increased heart rate.
- depressed mucociliary function which decreases clearance of secretions.

• Continue chronic therapy for pulmonary hypertension throughout the perioperative period such as chronic prostacyclin trepostinil infusion or chronic iloprost inhalation.

Intraoperative Management:

Aim:

• Avoid hypoxia, hypercarbia, histamine release, acidosis, and sympathetic stimulation.

• Avoid bradycardia as the stroke volume is limited by increased ventricular afterload.

• Avoid hypovolemia; maintain intravascular volume (preload) at normal or high levels to maintain cardiac output in the face of increased right ventricular afterload.

Monitoring:

Besides the standard monitors,

• Transesophageal echocardiography.

• Invasive arterial line for arterial blood pressure and blood gases.

• Central venous catheterization: A sudden increase in central venous pressure (and right atrial pressure) indicates right ventricular failure.

• Pulmonary artery catheterization to detect right ventricular and left ventricular function and can assess the response to the pulmonary vasodilator therapy.

• Nerve stimulator to allow smooth recovery.

Choice of Anesthesia:

a- Regional Anesthesia:

Advantages:

It avoids the effects of general anesthesia on respiration (e.g., decreased functional residual capacity, and ciliary activity, and increased ventilation/perfusion mismatching).

Disadvantages:

• It is not suitable for upper abdominal surgery which requires a high sensory level of anesthesia especially subarachnoid block which decreases systemic vascular resistance while pulmonary vascular resistance is still high due to the pulmonary hypertension. Therefore, this leads to severe systemic hypotension.

• It may cause loss of the function of the accessory muscles of respiration that may be very deleterious in patients with pulmonary diseases.

b- General Anesthesia:

Induction:

Smooth induction is required with:

- **Preoxygenation** 100% O_2 for 5 min.
- **Decreasing the pressor response** to intubation as before in the chapter of "Airway Management".
- Etomidate is a good choice and a small dose of thiopentone can be given safely. **Ketamine** should be avoided because it increases pulmonary vascular resistance.
- Avoid muscle relaxants which cause **histamine release** such as suxamethonium, atracurium, metocurine and d-tubocurarine; therefore, **vecuronium** or **cis-atracurium** is a good choice.

Maintenance:

A deep plane of anesthesia should be maintained to blunt sympathetic responses to surgical stimuli.

- **Volatile agents:** are bronchodilators; therefore, they are used safely, but should be used cautiously in patients with severe right ventricular failure as **they depress myocardial contractility**.
- N_2O: is avoided because it increases pulmonary vascular resistance. If it is used, it must be associated with close monitoring of its pulmonary effects.
- **Opioids**: **Avoid large doses** as they may produce postoperative respiratory depression.
  Avoid morphine as it may produce histamine release.
- **Muscle relaxants:** Avoid relaxants which cause histamine release.
  Vecuronium or cis-atracurium is of choice.
- **Mechanical ventilation:**
  - It improves oxygenation despite increasing the pulmonary vascular resistance.
  - **Avoid hyperventilation** because it causes hypocapnia which in turn causes secondary hypokalemia. The latter precipitates digitalis toxicity.
  - All inspired gases must be warmed and humidified.

Intraoperative Complications:

- **Systemic hypotension**: should be managed by decreasing anesthetics or applying vasopressors.
- **Increased pulmonary hypertension**: should be treated by pulmonary vasodilators.
- **Pregnant patients with pulmonary hypertension: Mortality** in these patients is **very high** (near 50%) during vaginal delivery. Mortality may even be higher when cesarean delivery is performed. Regional anesthesia is a very good choice, but with considering the above precautions.

Recovery and Extubation:

Smooth recovery is needed with proper returning of muscle activity which should be assessed by a nerve stimulator.

Postoperative Management:

Close monitoring is required (in intensive care units for high risk patients) to avoid complications such as:

- Right ventricular failure.
- Ischemia.
- Arrhythmias.
- Respiratory failure.

Therefore, O_2 must be given to all patients.
Postoperative ventilation might be needed.
Postoperative analgesia is essential to avoid unwanted sympathetic stimulation.

Cardiomyopathy

Definition (by the American Heart Association, 2006)

- Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilation and are due to a variety of causes that are frequently genetic.
- Cardiomyopathies are either confined to the heart (primary) or are a part of generalized systemic disorders (secondary), often leading to cardiovascular death or progressive heart failure-related disability.

Old Classification of Cardiomyopathies

1- Hypertrophic obstructive cardiomyopathy.
2- Dilated (ischemic) cardiomyopathy.
3- Restrictive cardiomyopathy.
4- Obliterative cardiomyopathy.

This classification does no longer exist in the new American Heart Association.

New Classification of Cardiomyopathies (by the American Heart Association)

A) Primary Cardiomyopathies: are those exclusively (or predominantly) confined to the heart muscle. They include:

1- Genetic:
- Hypertrophic cardiomyopathy.
- Arrhythmogenic right ventricular cardiomyopathy.
- Left ventricular non-compaction.
- Glycogen storage disease.
- Conduction system disease (Lenègre's disease).
- Ion channelopathies: long QT syndrome, Brugada syndrome, or short QT syndrome.

2- Acquired:
- Myocarditis (inflammatory cardiomyopathy), viral, bacterial, rickettsial, fungal, and parasitic (Chagas disease).
- Stress cardiomyopathy.
- Peripartum cardiomyopathy.

3- Mixed:
- Dilated cardiomyopathy.
- Primary restrictive non-hypertrophied cardiomyopathy.

B) Secondary Cardiomyopathies: are those demonstrating pathophysiological involvement of the heart in the context of a multiorgan disorder.

1- Infiltrative:
- Amyloidosis.
- Gaucher's disease.
- Hunter's syndrome.

2- Storage:
- Hemochromatosis.
- Glycogen storage disease.
- Neimann-Pick disease.

3- Toxic:
- Drugs: cocaine, alcohol.
- Chemotherapy drugs: doxorubicin, duanorubicin, cyclophosphophamide.
- Heavy metals: lead, mercury.
- Radiation therapy.

4- Inflammatory:
- Sarcoidosis.

5- Endomyocardial:
- Hypereosinophilic (Löffler's) syndrome.
- Endomyocardial fibrosis.

6- Endocrine:
- Diabetes mellitus.
- Hyper- or hypothyroidism.
- Pheochromocytoma.
- Acromegaly.

7- Neuromuscular:
- Duchenne-Becker dystrophy.
- Neurofibromatosis.
- Tuberous sclerosis.

8- Autoimmune:
- Lupus erythematosus.
- Rheumatoid arthritis.
- Scleroderma.
- Dermatomyositis.
- Polyarteritis nodosa.

The most common types of cardiomyopathies are discussed down.

1- Hypertrophic obstructive cardiomyopathy (HOCM). Its incidence is 1: 500 of general population. There are other names: Asymmetric septal hypertrophy, Idiopathic hypertrophic sub-aortic stenosis (IHSS), and Muscular sub-aortic stenosis.

2- Dilated cardiomyopathy.

3- Secondary cardiomyopathy with restrictive physiology.

	Hypertrophic Obstructive Cardiomyopathy (HOCM)	Dilated Cardiomyopathy	Secondary Cardiomyopathy with Restrictive Physiology
Cause	It is primary cardiomyopathy mainly **hereditary (genetic),** transmitted as an autosomal dominant disease resulting in increased Ca^{++} channel density which causes unexplained hypertrophy.	• It is primary mixed cardiomyopathy usually **idiopathic,** but may be **genetic** or associated **with infection** such as viral Coxsackie B infection. • Many types of secondary cardiomyopathies have the features of dilated cardiomyopathy such as cardiomyopathies due to **alcohol, cocaine, the peripartum state, pheochromocytoma, infectious diseases** (human immunodeficiency virus), **uncontrolled tachycardia, Duchenne's muscular dystrophy, thyroid disease, chemotherapy, radiotherapy, coronary artery diseases, hypertension, and vascular diseases.**	It is secondary cardiomyopathy due to infiltration of the myocardium by abnormal material such as: • Amyloidosis. • Hemochromatosis • Glycogen storage disease • Hypereosinophilic syndrome. • Carcinoid syndrome.
Pathology	There is **asymmetrical hypertrophy** of the **interventricular septum** and the anterolateral free wall of the left ventricle which causes: • **Dynamic outflow obstruction of the left ventricle;** the obstruction reaches peak in mid-to late systole and varies with heart beats hence the name **dynamic** (in contrast to fixed obstruction of the aortic stenosis). The obstruction is the result of narrowing in the subaortic area **caused by** a systolic anterior motion of the anterior mitral valve leaflet against the hypertrophied septum. Systolic anterior motion may be at least partly due to a Venturi effect drawing in the anterior leaflet during rapid ejection of the hypertrophied ventricle. The obstruction is **induced by** Valsalva maneuver. The obstruction **leads to**: ▫ **More myocardial hypertrophy**. ▫ **Diastolic dysfunction** due to diastolic stiffness with the abnormal hypertrophied myocardium. This leads to elevated left ventricular end-diastolic pressure which may result in **myocardial ischemia**. ▫ **Decreased cardiac output**. ▫ Mitral regurgitation due to interference with the movement of the MV leaflet by the hypertrophied interventricular septum. Clinical pictures: • Mainly females 50-70 year old, but all ages can be affected. • Asymptomatic. • Angina which is relieved by the recumbent position due to the effect of increased preload. • Congestive heart failure with its signs and symptoms such as exertional dyspnea and fatigue. • Tachyarrhythmias such as atrial fibrillation, ventricular fibrillation that may cause syncope and sudden death. • Harsh systolic murmur along the left sternal border which shows marked variation with Valsalva maneuver, nitroglycerin and standing-hypotension because these decrease the left ventricular size resulting in increased obstruction. This in turn increases the murmur.	There is **left ventricular or biventricular dilatation** which causes: • Functional mitral or tricuspid regurgitation. • Congestive heart failure. • Left ventricular hypokinesia and there may be mural thrombi which may produce systemic embolization. • Angina, first degree heart block, arrhythmias as atrial fibrillation. • Mortality occurs in 75% of cases.	There is **a decrease in ventricular compliance** (due to thickened endocardium) which causes: • Impaired diastolic filling which results in decreased cardiac output (as in constrictive pericarditis). • Arrhythmias. • Conduction disturbances. • Systemic embolization. • Mitral and tricuspid regurgitation are common.

Investigations LV = left ventricular EF = ejection fraction CO = cardiac output SV = stroke volume ↑ = increased ↓ = decreased	1- ECG: shows left ventricular hypertrophy in HOCM and ischemia is common finding. 2- Chest x-ray shows dilated heart in dilated cardiomyopathy. 3- Echocardiography: shows • Left ventricular hypertrophy. Provocative Valsalva or nitrate echocardiography can help in diagnosis in HOCM. • Dilated all chambers and global hypokinesia, segmental wall motion abnormalities, mural thrombus in dilated cardiomyopathy. 4- Cardiac catheterization shows increased left ventricular end-diastolic pressure. 5- Myocardial perfusion scan with thallium-201. 6- Endomyocardial biopsy and DNA analysis are definitive diagnostic investigations but are rarely used.		
	• LV contractility (EF) ↑↑ • CO (and SV) ↑ • Ventricular compliance ↓	↓ ↓ ↑	↓ ↓ ↓
Treatment	**A) Factors maintaining left ventricular size (decreasing outflow obstruction):** **1- Decrease the contractility** by β-blockers, Ca^{++} channel blockers such as verapamil, or disopyramide. They should continue perioperatively. Therefore, volatile anesthetics are a good choice during anesthesia. **2- Increase the preload** by maintaining relative hypervolemia, bradycardia, and avoiding vasodilators and high positive pressure mechanical ventilation. **3- Increase the afterload** by α-agonists such as phenylephrine (they increase systemic vascular resistance without increasing the contractility) and by maintaining blood pressure to the upper normal levels (so avoid vasodilators and hypotension). **B) Treatment of complications such as atrial fibrillation and angina.** **C) Septal myomectomy or myotomy** by cardiopulmonary bypass surgery.	1-**Treatment of the cause**: e.g., total abstinence from alcohol, immuno-suppressive treatment as corticosteroids or azathioprine, or coronary revascularization. **2- Treatment of congestive heart failure** such as avoiding unnecessary physical activity, weight control, low sodium diet, drugs as digoxin, diuretics, inotropes, and vasodilators. **3- Treatment of complications** as arrhythmias, mural thrombosis (by anticoagulants). **4- Cardiac transplantation**: Dilated cardiomyopathy is the main indication of transplantation.	• **No effective treatment** is present. • **Treatment of complications** such as congestive heart failure and arrhythmias may be indicated. • N.B.: Cardiac transplantation is not a therapeutic option because myocardial infiltration will recur in the transplanted heart.
Anesthetic management	It is the same anesthetic principles as **aortic stenosis.** Arterial pressure waveform shows **Bisferiens pulse**; bifid initial rapid peak due to early unobstructed ventricular ejection followed by a subsequent decrease and a 2nd peak that are due to dynamic obstruction.	It is the same anesthetic principles as **mitral regurgitation or congestive heart failure**.	It is the same anesthetic principles as cardiac tamponade and constrictive pericarditis.

Heart Failure (Ventricular Dysfunction)

Definition

Inability of the heart to pump a sufficient amount of blood to meet the body's metabolic requirements.

Causes

a) Left Ventricular Failure:
- Valvular heart disease.
- Ischemic heart disease (myocardial infarction).
- All types of cardiomyopathy: They are discussed above.
- Systemic hypertension.
- Pericardial disease.
- Severe arrhythmias.

b) Right Ventricular Failure:
- Secondary to left ventricular failure.
- Corpulmonale: It is discussed above.
- Right ventricular ischemia or infarction.

Forms of Heart Failure

Heart failure is described as
- Systolic or diastolic.
- Acute or chronic.
- Left sided or right sided.
- High output or low output.

Early in the course of heart failure, the various forms have **different clinical** and therapeutic implications, but **late in the course** of heart failure, **all forms** of heart failure **develop high ventricular end-diastolic pressure** due to altered ventricular function and neuro-hormonal regulation and **congestive heart failure** occurs.

A) Systolic and Diastolic Heart Failure:

	Systolic Heart Failure	Diastolic Heart Failure
Definition	• It is defined as decreased ventricular systolic wall motion. It reflects the ability of the left ventricle to empty. • It describes the contraction phase of myocardial performance i.e., **inotropic function.** • It is related to **the release of Ca^{++}** from the sarcoplasmic reticulum and its movement into cells.	• It is defined as abnormal ventricular relaxation and reduced compliance. • It describes the relaxation phase of myocardial performance i.e., **lusitropic function.** • It is related to the **uptake of ionized Ca^{++}** into the sarcoplasmic reticulum
Age and sex	Typically 50-70 years old More often **males**	The incidence increases with age 15% in age < 45 years 35% in age 50-70 years > 50% in age > 70 years More often **females**
Patho-physiologic changes LV = left ventricular ED = end-diastolic EF = ejection fraction	• LVED volume is increased. • LVED pressure is increased. • LVEF is decreased ≤ 40%. There are two types of EF: ▫ Emptying EF (both forward and back-ward blood flow). It is high in mitral regurgitation. ▫ Effective EF (only forward blood flow). It is low in mitral regurgitation. This is the most important in assessing the systolic function of the heart. • LV cavity size is usually dilated. • Causes: Systolic heart failure is due to: usual coronary artery diseases, dilated cardiomyopathy, chronic pressure overload (aortic stenosis, chronic hypertension), and chronic volume overload (mitral and aortic regurgitation and high output heart failure) with left bundle branch block.	• LVED volume is decreased. • LVED pressure is increased. • LVEF is preserved ≥ 40%. • LV cavity size is usually normal, often with concentric LV hypertrophy. • Classification: Diastolic heart failure is classified into 4 stages or patterns as follows: Class I (abnormal relaxation pattern): is characterized by an abnormal LV relaxation pattern with normal left atrial pressure and ventricular compliance. Class II (reversible restrictive pattern): is characterized by abnormal relaxation with decreased LV compliance (i.e., restrictive pattern) resulting in an increase in LVED pressure. This is a reversible stage. As a compensatory mechanism, the pressure in the left atrium increases, so that LV filling can occur despite the increase in LVED pressure. Class III (irreversible restrictive pattern): is characterized by absence of preload reduction in spite of nitrates or Valsalva maneuver. Class IV: is the most severe form.
Clinical signs and symptoms	They do not reliably differentiate systolic dysfunction from diastolic dysfunction	
Investigations	• **ECG:** atrial fibrillation is usually present. **Gallop rhythm and 3rd heart sound** are usually present. • **Chest radiography:** Congestion and cardiomegaly. • Echocardiography, radionuclide imaging, or ventriculography can assess the LVEF and LV cavity sizes.	• **ECG:** atrial fibrillation is usually paroxysmal. **Gallop rhythm and 4th heart sound** are usually present • **Chest radiography:** congestion ± cardiomegaly. • Echocardiography, radionuclide imaging, or ventriculography can assess the LVEF and LV cavity sizes.

B) Acute and Chronic Heart Failure:

Acute Heart Failure: is defined as either:

• **a sudden** change in the signs and symptoms of chronic heart failure requiring emergency therapy or • a sudden onset of clinical picture of heart failure in a patient with no previous history of heart failure.

Pathology:

The hemodynamics of acute heart failure include high ventricular filling pressures, and **a sudden decrease in cardiac output**, but the **blood pressure** can be normal, hypertensive, or hypotensive (acute

heart failure with hypotension is called **Cardiogenic Shock** without signs of peripheral edema. There is sudden pathology which induces the acute heart failure such as

- large myocardial ischemia or infarction
- acute valve dysfunction (stenosis or regurgitation)
- cardiotoxic drugs
- terminal heart failure which is refractory to therapy
- volume overload as renal impairment or hypoalbuminemia.
- acute myocarditis
- sepsis
- alcohol
- severe hypertensive crisis

Chronic Heart Failure: is present in patients with a long standing cardiac disease. Chronic heart failure is accompanied by **venous congestion and peripheral edema**, but **blood pressure** is typically **maintained**.

C) Left-Sided or Right-Sided Heart Failure:

	Left-Sided Heart Failure	Right-Sided Heart Failure
End diastolic pressure	Increased left ventricular end-diastolic pressure	Increased right ventricular end-diastolic pressure
Filling pressure	Increased pulmonary capillary wedge pressure > 18 mm Hg	Increased central venous pressure > 15 mm Hg
Congestion	Pulmonary venous congestion (± systemic congestion (peripheral edema)	Systemic venous congestion

D) Low-Output or High-Output Heart Failure:

	Low-Output Heart Failure	High-Output Heart Failure
Pathology	There is limited or even absent ability to increase cardiac output in response to vasodilatation, exercise, or stress i.e., **low fixed cardiac output**. It is the common end point of all causes of heart failure. There is an **increase in the systemic vascular resistance**.	There is **hyperdynamic or hypermetabolic** state with a **decrease in the peripheral vascular resistance.**
Causes	The most common causes are coronary artery diseases, cardiomegaly, hypertension, valvular diseases, pericardial diseases, pulmonary hypertension, pulmonary embolism, or complete heart block.	The most common causes are anemia, pregnancy, arterio-venous fistulas, severe hyperthyroidism, beriberi, fever, sepsis, or Paget's disease of the bone.

Adaptive Patho-Physiological Mechanisms

The heart failure passes in three stages:

	Cardiac Filling Pressure	Stroke Volume (SV) and Heart Rate (HR)	Cardiac Output (CO)	Heart Failure Status
Stage I: At early stage	↑	Maintained	Maintained	Compensated heart failure
Stage II: In the next stage	↑	SV ↓ and HR ↑ due to compensatory mechanisms.	Maintained as (CO = SV X HR)	Compensated heart failure
Stage III: In the final stage	↑	SV ↓↓ and HR ↑↑	↓	Decompensated heart failure

In the early stages of heart failure (compensated), the cardiac output is normal and maintained.
In the late final stage of heart failure (decompensated), the cardiac output falls and irreversible shock occurs with tissue underperfusion which stimulates ischemic mediators; therefore, more myocardial and peripheral tissues injury and damage occur.
The compensatory mechanisms include:

1- Frank-Starling Mechanism:

Significant impairment of ventricular diastolic function produces ventricular dilatation (right ventricular dilatation does not necessarily occur). This increases ventricular end-diastolic volume (VEDV) which in turn increases ventricular end-diastolic pressure (VEDP) (because the tension developed by the contracting muscle is greater when the resting length of that muscle is increased). Increase in VEDV results in:

- an increase in stroke volume which in turn increases cardiac output.
- stimulation of atrial mechanoreceptors which in turn stimulate the SA node and result in increased heart rate.

Finally, when heart failure ensues, the myocardial fibers are unable to generate any further increase in the force of contraction leading to decreased stroke volume and a rapid decrease in cardiac output.

2- Sympathetic Nervous System Activation:

There is increased sympathetic activity (the associated hypotension results in inhibition of the baroreceptors leading to baroreceptor reflex) due to increased norepinephrine release from nerve endings or from the adrenal medulla which results in:

1. Increased heart rate and contractility:

Increased contractility i.e., increased velocity of contraction is developed by the cardiac muscle and the maximum velocity of contraction (V_{max}).

Increased heart rate:

- It is accompanied by increased contractility; this is known as the **rate-treppe phenomenon.**
- In the presence of systolic heart failure and low basal cardiac output (CO), the stroke Volume (SV) is relatively fixed; therefore, increased heart rate (HR) results in increased cardiac output (CO = HR x SV).

In diastolic heart failure, increased heart rate can produce a decrease in cardiac output due to inadequate ventricular filling time. Therefore, control of heart rate is important in treatment of diastolic heart failure.

2. Arteriolar constriction:

It serves to maintain arterial blood pressure despite a decrease in cardiac output, but actually it causes more ventricular dysfunction.

It also causes redistribution of blood from the kidneys, splanchnic organs, skeletal muscles and skin so as to maintain cerebral and coronary blood flow despite a decrease in cardiac output.

3. Venous constriction:

It shifts blood from the peripheral sites to the central circulation. This increases venous return and maintains cardiac output by Frank-Starling mechanism.

- These compensatory responses may be effective in the short term, but they contribute to the deterioration of heart failure in the long term. For example, fluid retention, increased venous return, and increased afterload can impose more work on the failing myocardium, increase myocardial energy expenditure, and further reduce cardiac output and tissue perfusion.
- Finally, chronic activation of the sympathetic system leads to:
  - Catecholamine depletion.
  - Decreased adrenergic receptors numbers (i.e., down-regulation).
  - Decreased adrenergic receptors response to catecholamines i.e., decreased sensitivity.

Therefore, the failing heart becomes dependent on circulatory catecholamines. On abrupt withdrawal of sympathetic outflow or decrease in circulatory catecholamines (as during induction of anesthesia), acute cardiac decompensation may occur.

As heart failure progresses, vasoconstriction becomes more due to more sympathetic stimulation, high levels of circulating vasopressin, endothelial dysfunction, and release of inflammatory mediators.

3- Hormonal Mediated Responses:

• Renin-angiotensin system:

Decreased cardiac output secondary to ventricular dysfunction decreases renal blood flow. This stimulates β_1 receptors which in turn stimulates the renin-angiotensin system. The latter causes:

- Increased angiotensin II which produces vasoconstriction; therefore, a further increase in afterload occurs with further deterioration of heart failure.
- Secondary increased aldosterone which produces Na^+ and H_2O retention; therefore, the blood volume increases and improves pump function initially through Frank-Starling mechanisms.

• Anti-Diuretic Hormone (ADH):

With right-sided heart failure, systemic venous congestion shifts H_2O from the intravascular compartment to the interstitial compartment. This causes edema formation and increases plasma osmolarity. The latter stimulates osmoreceptors in the hypothalamus which secretes ADH. ADH causes H_2O retention, increases blood volume, and improves pump function initially by increased venous return through Frank-Starling mechanism.

• Natriuretic peptides: There are two types:

a- Atrial Natriuretic Peptide (ANP):

It is stored in atrial muscles and released in response to increased atrial pressure and increased atrial distension (produced by tachycardia and hypervolemia).

b- Brain type (B-type) natriuretic peptide (BNP):

It has been recently discovered. It is secreted by both the atrial and ventricular myocardium in response to ventricular volume and pressure overload. In failing heart (left- or right-sided), the ventricle becomes the

principal site for BNP production. Plasma levels of BNP increase in direct relation to increases in ventricular end-diastolic volume and pressure (both left- and right-sided).
Both natriuretic peptides (ANP and BNP) promote blood pressure control and protect the cardiovascular system from the effects of volume and pressure overloads. They cause:

1- Potent vasodilatation which antagonizes the effect of angiotensin II.
2- Increased glomerular filtration rate which produces natriuresis and diuresis.
3- Decreased aldosterone and ADH secretion.
4- Anti-hypertrophy and anti-inflammatory actions and inhibition of sympathetic nervous system.

The effect of natriuretic peptides is decreased over time in heart failure, but exogenous administration of BNP is useful in treatment of acute heart failure.

4- Myocardial Remodeling:

It is the process by which mechanical, neuro-hormonal, and genetic factors change the left ventricular size, shape, and function. The process includes:

a- Myocardial hypertrophy:

It is a compensatory mechanism that develops in response to chronic **pressure** overload i.e., afterload (such as aortic stenosis, pulmonary hypertension, or systemic hypertension). So, the ratio of the ventricular wall tension to the ventricular radius is increased. This means, that in a failing heart, there is an increase in the radius which increases wall tension. Myocardial hypertrophy increases myocardial contractility which in turn increases stroke volume. This causes increased cardiac output.
Law of La Place states that $2T = P \times r$
Where: T = ventricular wall tension, P = intraventricular pressure, and r = radius of chamber

b- Myocardial dilation and wall thinning:

It is a compensatory mechanism that develops in response to chronic **volume** overload (such as mitral regurgitation or aortic regurgitation), later on hypertrophy occurs. So, the ratio of ventricular wall tension to ventricular radius is unchanged. Cardiac dilation increases stroke volume and cardiac output according to Frank-Starling's mechanism.
Finally, myocardial hypertrophy (increased muscle bulk) and cardiac dilation (increased wall tension according to the law of Laplace) increase myocardial O_2 demand. Both decrease cardiac efficiency.
N.B.: Acute severe afterload changes (severe systemic hypertension or severe pulmonary vasoconstriction) may cause ventricular distension. This increases wall tension to a failure threshold with subsequent acute left or right ventricular failure.

c- Increased interstitial collagen deposition.

d- Myocardial fibrosis and scar formation due to myocyte death.

The most common cause of myocardial remodeling is ischemic heart injury, and it encompasses both hypertrophy and dilation of the left ventricle.
N.B.: Angiotensin-converting enzyme inhibitors (ACEIs) have been proven to promote a "reverse-remodeling" process. Therefore, they are the first-line therapy for heart failure.

Clinical Pictures

Severity:

The severity of heart failure can be classified according to the clinical picture mainly dyspnea and fatigue according to the **New York Heart Association (NYHA) classification.** It is discussed above.
The American College of Cardiology and the American Heart Association published the 2005 guideline update for the diagnosis and management of chronic heart failure and introduced **a new classification** based on the progression of the disease. This classification is complementary to the New York Heart Association classification and is used in guiding therapy. The classification includes 4 stages:

Stage A: patients at high risk of heart failure, but without structural heart disease or symptoms of heart failure.
Stage B: patients with structural heart disease, but without symptoms of heart failure.
Stage C: patients with structural heart disease with previous or current symptoms of heart failure.
Stage D: patients with refractory heart failure requiring specialized interventions.

I- Clinical Picture of Low Cardiac Output (in Both Left and Right Heart Failure):

These symptoms should be related to the level of activity.
Muscle: fatigue, weakness, and exhaustion (it is very common in patients with heart failure).
Central nervous system: dizziness, syncope, confusion, anorexia, nausea, and insomnia.

Kidney: oliguria (prerenal azotemia characterized by a disproportionate increase in blood urea nitrogen relative to s. creatinine) and necturia (it may contribute to insomnia).
Heart: angina pectoris (chest pain).
Peripheral extremities: cool, sweaty, and pale.

II- Clinical Picture of Left Ventricular Failure:

a. Pulmonary venous congestion:

- **Dyspnea** (exertional then at rest), **orthopnea** (dyspnea on recumbent position), and orthopneic **dry non-productive cough**.
- **Paroxysmal nocturnal dyspnea** (and wheeze): is shortness of breath that awakens the patient from sleep. This symptom must be differentiated from anxiety-provoked hyperventilation or wheezing due to accumulation of secretions in patients with chronic bronchitis as paroxysmal nocturnal dyspnea and wheeze caused by pulmonary congestion (i.e., cardiac asthma) are accompanied by radiographic evidence of pulmonary congestion.
- **Acute pulmonary edema**, if occurs, starts with fine basal rales and then progresses to diffuse rales in severe cases of acute pulmonary edema causing pink or whitish frothy sputum and expiratory wheezes.
- **Tachypnea and cyanosis** especially in lips and nail beds.

b. Left cardiac signs:

- Tachycardia.
- S_3 gallop (ventricular diastolic gallop): It is produced by blood entering and distending a relatively noncompliant left ventricle.
- Murmurs of mitral regurgitation, aortic stenosis, or aortic regurgitation.

c. Symptoms of the cause e.g., chest pain.

III- Clinical Picture of Right Ventricular Failure:

a. Systemic venous congestion:

- Peripheral **bilateral edema** (dependent and pitting).
- **Jugular venous distension** with a prominent a wave may be present or induced by pressing on the liver (**hepato-jugular reflux**).
- **Hepatomegaly** with right hypochondrial (upper quadrant) pain and tenderness. Jaundice may occur in severe cases.
- **Kussmaul's sign**: during inspiration, there is an increase in the jugular venous distension and pressure (normally during inspiration, there is increased negative intrathoracic pressure which propels jugular blood to the pulmonary circulation easily resulting in decrease of jugular venous pressure). The Kussmaul's sign occurs also in constrictive pericarditis and cardiac tamponade.
- Marked weight loss, also known as cardiac cachexia, is a sign of severe chronic heart failure. It is caused by - an increase in the metabolic rate,
  - anorexia and nausea,
  - decreased intestinal absorption of food caused by splanchnic venous congestion,
  - high levels of circulating cytokines.
- Pleural effusions (usually right-sided) may be present.

b) Right cardiac signs:

- Para-sternal heave along the left sternal border.
- Increased pulmonary component of S_2.
- S_4 gallop.
- Possible murmur of tricuspid and pulmonary regurgitation.

c) Symptoms of the cause e.g., left ventricular failure (the most common cause) or underlying pulmonary diseases such as dyspnea, cough, and expectoration.

Investigations

a- To Detect the Cause of the Heart Failure:

ECG, chest x-ray, echocardiography, radionuclide angiography …etc (as discussed before in ischemic and valvular heart diseases).

b- To Detect Sequelae of Heart Failure: such as hypotension and shock.

Arterial blood gases show hypoxemia or metabolic acidosis (lactic acidosis). Renal and hepatic function tests may be abnormal.

General Assessment of Cardiac Function: includes

- tissue perfusion assessment,
- central venous pressure assessment,

- pulmonary artery catheter (for derived hemodynamics),
- cardiac output measurement,

and • transesophageal echocardiography.

They are discussed in details in chapter "Monitoring for Anesthesia & Intensive Care".

N.B.: Indicators of Significant Ventricular Dysfunction (Bad Ventricular Function):

- Left ventricular ejection fraction < 50% (0.5). It is the most important.
- Left ventricular end-diastolic pressure > 18 mm Hg.
- Cardiac index < 2 - 2.2 L/min/m^2.
- Marked or multiple wall motion abnormalities.

Management of Heart Failure

The management of heart failure differs according to the type of heart failure as:

- Management of chronic heart failure (systolic or diastolic).
- Management of acute heart failure (usually systolic).
- Management of high cardiac output heart failure.
- Management of right-sided heart failure with or without pulmonary hypertension.

A) Management of Chronic Heart Failure:

I- Lifestyle Modification: includes

- Smoking cessation.
- A healthy diet with moderate Na^+ restriction.
- Fluid restriction of 1-2 L/day with monitoring of fluid balance by daily weighing.
- Weight control.
- Aerobic exercise.
- Moderate alcohol consumption.
- Adequate glycemic control.
- Annual immunization for infleunza and pneumococci.

II- Pharmacological Management:

a- Systolic Heart Failure:

Combination of pharmacology is common.

i) Disease-Modifying Therapy:

1- Angiotensin-Converting Enzyme Inhibitors (ACEIs): They are the first choice because they decrease mortality and morbidity of patients in any stage of heart failure.

2- Angiotensin II Receptor Blockers: They are recommended for patients who cannot tolerate ACEIs.

3- Aldosterone Antagonists: as spironolactone

4- β-blockers: especially bisoprolol, carvedilol, and metoprolol. They decrease morbidity and mortality of heart failure.

5- Vasodilators: as hydralazine or nitrates as they decrease afterload and thus the increase the ejection fraction.

ii) Symptomatic Therapy:

1- Diuretics: especially thiazide and/or loop diuretics

2- Digitalis (Digoxin): It is added to the standard therapy when patients are still symptomatic despite maximal treatments with diuretics, ACEIs, and β-blockers. It is also used in patients with atrial fibrillation associated heart failure to control ventricular rate. Care should be taken for digitalis toxicity.

iii) Other Pharmacological Therapy:

1- Aspirin.

2- Warfarin in patients with atrial fibrillation or known left ventricular thrombus.

3- Statins: They decrease morbidity and mortality by their antiinflammatory and lipid-lowering effects.

4- Allopurinol.

5- Erythropoietin and i.v. iron in anemic patients.

For actions, doses, side effects of the above drugs, see the chapter of "Pharmacological adjuncts for Anesthesia & Intensive Care".

b- Diastolic Heart Failure:

As the systolic function is normal, positive inotropic agents have no role in the treatment of diastolic heart failure.

i) Decrease Risk Factors: to prevent development of diastolic heart failure such as:

- Treat coronary artery diseases as by coronary revascularization.

- Treat hypertension.
- Control weight gain.
- Treat diabetes mellitus.

ii) Decrease Heart Rate to Allow Adequate Filling Time of the Left Ventricle:

- β-blockers.
- Ca^{++} channel blockers especially diastolic heart failure due to idiopathic hypertrophic cardiomyopathy.
- Digoxin.

iii) Restore and Maintain Sinus Rhythm to Allow Adequate Filling Time of the Left Ventricle:

- Cardioversion.
- Amiodarone.
- Digoxin.

iv) Control Volume Overload:

- Diuretics.
- Vasodilators especially nitroglycerin and milrinone. They also have lusitropic actions that promote ventricular relaxation during diastole.
- Low-sodium diet.

v) Decrease Ventricular Remodeling:

- ACEIs
- Statins.

III- Surgical Management of Heart Failure:

1- Percutaneous coronary interventions or coronary artery bypass grafting surgery for ischemia.
2- Corrective valve surgeries.
3- Ventricular aneurysmectomy i.e., ventricular remodeling surgery to remove ventricular scar after myocardial infarction.
4- Ventricular assist devices (extracorporeal membrane oxygenator "ECMO" or implantable pulsatile devices).
5- Heart transplantation.
6- Cardiac resynchronization therapy:
   - It is indicated in patients with heart failure who have a ventricular conduction delay (QRS prolongation on ECG between 120-150 msec) and ejection fraction < 35% as this conduction delay creates a mechanical dys-synchrony that impairs ventricular function.
   - It is biventricular pacing that consists of the placement of a dual-chamber cardiac pacemaker, but with an additional lead introduced into the coronary sinus/ coronary vein until it reaches the dys-synchronous left ventricular wall. With this lead in place, the heart contracts more efficiently and ejects a large cardiac output.
7- Implanted cardioverter/defibrillators (ICDs): They prevent sudden death in patients with heart failure especially with ejection fraction < 30% or ejection fraction < 40% and their electro-physiologic study demonstrates inducible ventricular dysrhythmias.

B) Management of Acute Heart Failure: (it is usually of systolic type)

Acute heart failure can occur preoperatively or even intraoperatively which necessitates emergency treatment. The management of acute heart failure is usually conducted by anesthesiologists in operating rooms or by intensivists in the intensive care units.

I) General Measures:

1- Oxygen.
2- Bed rest.
3- Correction of anemia and fever.
4- Noninvasive positive pressure mechanical ventilation (without endotracheal intubation) by using tight-fitting masks can be used e.g., continuous positive airway pressure (CPAP) is usually required in most patients.
Invasive mechanical ventilation (with endotracheal intubation) is usually not necessary except in severe cardiogenic pulmonary edema.

II) Management According to the Associated Blood Pressure:

a- Treatment of Acute Heart Failure with Normal Blood Pressure:

1- Inotropic therapy by **dobutamine** (it is more preferred than other inotropic agents as it has a minimal chronotropic and vasoconstrictive effects). **Inodilator therapy** by **milrinone** or **milrinone** (phosphodiesterase inhibitors), or **vasodilator therapy** by **nitroglycerin**.

2- Diuretics especially **loop diuretics** if the pulmonary capillary wedge pressure remains above 20 mmHg.

b- Treatment of Acute Heart Failure with High Blood Pressure:

1- **Vasodilator therapy**: with **nitroprusside or nitroglycerin**. Start with small doses and then titrate the dose according to the response. Nitroglycerin in addition, dilates coronary vessels.

2- Diuretics especially **loop diuretics** if the pulmonary capillary wedge pressure remains above 20 mmHg. High doses are required to relieve the symptoms rapidly as **i.v. furosemide 10-80 mg** and can be **repeated**. Some authors recommend furosemide as **i.v. infusion** instead of i.v. boluses because it produces vigorous diuresis especially **in furosemide resistance** (e.g., when 80 mg is given as an i.v. bolus, it results in less than 2 liters of urine output in the ensuing 4 hours). The i.v. infusion is more effective than i.v. boluses because the diuretic effect of furosemide is more closely related to its urinary excretion rate than to its plasma concentration. The dose of i.v. infusion of furosemide is as follows; start with **100 mg i.v. bolus as a loading dose** and followed by **40 mg/hour**. Double the dose rate every 12 hours if it is needed to achieve urine output of at least 100 mL/hour. The maximum dose is 169 mg/hour.

c- Treatment of Acute Heart Failure with Low Blood Pressure (Cardiogenic Shock):

1- **Dopamine, dobutamine, epinephrine, or norepinephrine** in vasoconstrictor doses.

2- **Mechanical assist devices** as a temporary measure such as intra-aortic balloon pump or left ventricular and/or right ventricular assist devices.

N.B.: **Digoxin** is of little importance in the treatment of acute heart failure and cardiogenic shock. It is only used for the treatment of atrial fibrillation with rapid ventricular response.

Isoproterenol is of little importance in the treatment of acute heart failure and cardiogenic shock. It is only used if there is bradycardia or severe aortic regurgitation (insufficiency).

III) Other New Therapeutic Regimens:

1- Calcium Sensitizers: such as **levosimendan:** It acts by increasing sensitivity of troponin C to intracellular Ca^{++}; therefore, it increases contractility without increasing intracellular Ca^{++} and thus there is no significant increase in myocardial O_2 consumption or heart rate and no propensity for dysrhythmias. It acts as inodilator as it increases contractility and produces systemic, pulmonary, and coronary vasodilation through vascular K-ATPase channels.

2- Exogenous B-type Natriuretic Peptide (BNP):

Nesiritide (*Natrecor*) is recombinant human BNP that binds to both the A- and B-type natriuretic receptors. It promotes arterial, venous, and coronary vasodilation by increasing cGMP, thereby decreasing left ventricular end-diastolic pressure and improving dyspnea. It induces diuresis and natriuresis. It has many effects similar to nitroglycerin, but it has no advantages over nitroglycerin and may increase short-term mortality; therefore, its value may be unproven.

Dose: loading i.v. bolus 2 µg/kg followed by i.v. infusion of 0.01 µg/kg/min for less than 48 hours. The dose can be increased 0.01 µg/kg/min every 3 hours to a maximum dose 0.03 µg/kg/min.

3- Nitric Oxide Synthetase Inhibitors:

N-nitro-L-arginine methyl ester (L-NAME) is still under investigation. It inhibits NO production which increases in heart failure. Heart failure stimulates the inflammatory cascade resulting in production of a large amount of NO in the heart and vascular endothelium. NO produces a negative inotropic and profound vasodilatory effect leading to cardiogenic shock and vascular collapse.

4- Patients with Renal Failure: Ultra-filtration or dialysis may be indicated to remove excess fluid.

Finally, after optimizing hemodynamic variables of acute heart failure with intravenous medications and attaining a period of stability, a gradual change to oral medications is appropriate by starting the oral medications and gradually decreasing i.v. agents.

All the above drugs are discussed in details in the chapter of "Pharmacological Adjuncts to Anesthesia & Intensive Care".

C) Management of High Cardiac Output Heart Failure:

Treatment is mainly directed to the cause such as:

- Anemia
- Sepsis
- Thiamine deficiency,
- Hyperthyroidism
- Fluid overloads that need diuretics or hemo-ultrafiltration.

D) Management of Right-Sided Heart Failure with/without Pulmonary Hypertension:

It is discussed before.

Anesthetic Management

Preoperative Management:

Preoperative Evaluation:

1- Clinical Picture (history and examination): of heart failure is discussed above.

Determination of the Operative Risk can be done as follows:

- NYHA classes I or II have only a slight risk of developing postoperative pulmonary edema.
- NYHA classes III or IV have an extremely high risk of developing postoperative pulmonary edema.
- Elective surgery should be postponed till adequately controlling the heart failure.
- Emergency surgery requires transferring patients to a major medical centre where careful invasive monitors should be used to optimize the preload, afterload and left and right ventricular stroke work.

2- Preoperative Investigations:

1. **Chest X-ray** (postero-anterior and lateral views): It gives an idea about:

- The size and shape of the cardiac shadow such as cardiomegaly.
- The underlying disease such as pulmonary edema.
- Radiographic signs of left ventricular failure include the following:
  - The earliest sign is pulmonary venous congestion in the basal lobes of the lungs.
  - Peri-vascular edema appears as hilar or peri-hilar haze. The hilus appears large with ill-defined margins.
  - Interlobar (septal) edema is called **Kerley's lines**:
    - Kerley A lines in the upper lung fields.
    - Kerley B lines in the lower lung fields.
    - Kerley C lines in the basal lung fields which appear as a honey-comb appearance.
  - Alveolar edema appears as a butterfly pattern of homogenous opacity.
  - Pleural and pericardial effusion (especially if biventricular failure is present).

N.B.: Radiographic signs of pulmonary edema may be delayed after the acute increase in left atrial pressure and clinical evidence of pulmonary edema by up to 12 hours. Also radiographic signs of pulmonary congestion may persist 1-4 days after normalization of cardiac filling pressure and resolution of the symptoms.

2. Twelve-Lead ECG:

It shows the underlying cardiac disease such as previous myocardial infarction, left ventricular hypertrophy, conduction abnormalities, and arrhythmias as atrial fibrillation or ventricular fibrillations.

3. Plasma (serum) B-type natriuretic peptide (BNP):

Value:

- The plasma BNP level has been used as a **biomarker for heart failure** and has proven to be an important tool for the **diagnosis** of heart failure (right or left).
- Plasma BNP levels show a direct **correlation with the severity** of heart failure i.e., plasma levels are higher in patients with more advanced stages of heart failure.
- It is also used as a monitoring tool to **assess the clinical course** of heart failure and **the effectiveness of treatment** of heart failure for patients who develop fluid overload.

BNP Levels:

- Plasma BNP levels < 100 Pg/mL indicate that heart failure is unlikely (90% negative predictive value).
- Plasma BNP levels **100-500 Pg/mL** suggests an intermediate probability of heart failure (84% positive predictive value).
- Plasma BNP levels **> 500 Pg/mL** are consistent with heart failure (90% positive predictive value).

Technique:

Plasma BNP can be rapidly assessed as a bedside test using a fluorescence immunoassay kit that allows easy identification of heart failure in the emergency department.

Factors affecting BNP levels:

Plasma BNP levels are affected by other factors such as **sex** (50% higher in females than males), advanced **age**, **renal** clearance (higher in renal insufficiency as BNP is cleared by the kidney), **obesity, pulmonary embolism, arterial fibrillation, and/or tachyarrhythmias** which can increase plasma BNP level, but less than 100 Pg/mL (in contrast to volume overload and heart failure that increase plasma BNP levels above 100 Pg/mL). Therefore, these factors have an impact on the interpretation of BNP levels.

Condition	Mean plasma BNP (Pg/mL)
• Female normal values at age 55-64 years	32
> 75 years	78
• Male normal values at age 55-65 years	20
> 75 years	48
• Renal insufficiency without volume overload	80
with volume overload	180
• Hear failure mild	186
moderate	791
severe	2013

4. Two-dimensional Echocardiography with Doppler flow: It is the most useful test
It shows the underlying cardiac disease and severity of failure. It can detect the left ventricular ejection fraction for systolic dysfunction and left ventricular filling and left atrial pressure for diastolic dysfunction.

5. Cardiac catheterization:
It shows the underlying cardiac disease and severity of failure.

6. Other Investigations:
- Renal function tests show a disproportionate decrease in serum urea compared to serum creatinine i.e., prerenal azotemia.
- Hepatic function tests show increased liver enzymes levels and prolongation of prothrombin time (PT).
- Arterial blood gases may show hypoxemia.
- Electrolyte assessment shows hypomagnesemia, hypokalemia, and hyponatremia.

Preoperative Preparation:

1- Treatment of All Precipitating Factors of Heart Failure: should be performed before elective surgery.

2- Preoperative Medications of Heart Failure:
- **β-blockers** should be maintained till the day of surgery.
- **Digoxin** can be continued until the day of surgery.
- **Diuretics** should be discontinued on the day of surgery.
- **ACEIs and angiotensin receptor blockers** should be discontinued one day before surgery to avoid excessive hypotension with anesthesia.

3- Premedications:
1- Sedatives: should be decreased or omitted to avoid ventilatory depression and tissue hypoxia.
2- Anticholinergics should be omitted to avoid their tachycardiac effect.

Intraoperative Management:

Aim: The same anesthetic principles **as mitral regurgitation** with avoiding further sympathetic stimulation as regurgitant valves and heart failure share in the features of low contractility.

1. Keep **the heart rate at slight tachycardiac levels** and avoid bradyarrhythmias and severe tachyarrhythmias.
2. Keep **blood pressure at low normal levels** to decrease the afterload, but avoid severe reduction or elevation of blood pressure.
3- Keep **normovolemia or slight hypovolemia**, but avoid severe decrease in the blood volume and preload.
3. Keep and **preserve myocardial contractility** and avoid myocardial depression.
4. **Avoid excessive sympathetic stimulation**.

Monitoring:

The same intraoperative monitors for patients with cardiovascular diseases are applied. They are discussed in intraoperative management of **hypertension** (see before).

Choice of Anesthesia:

A. Regional Anesthesia:
It is advised because the sympathetic blockade of regional anesthesia may produce vasodilatation which decreases the pre- and afterload, but **high blocks should be avoided.**

B. General Anesthesia:

Induction:
Preoxygenation with 100% O_2 for 5 min is essential.

Induction agents:

- **Etomidate** is of **choice** as it has little effects on cardiac function.
- **Ketamine** (usually with midazolam) can be used, but in the end-stage heart failure, the endogenous catecholamine stores are depleted and additional cardiac decompensation may occur after administration of ketamine due to its direct negative inotropic effect.
- **Large dose opioids** can be used as fentanyl 50 μg/kg i.v. or sufentanil 2-7 μg/kg i.v, but with the following **precautions**:
  - Apparent cardiac depression may occur with pure high-dose opioid induction; this likely represents withdrawal of an elevated baseline sympathetic tone (due to the stimulatory effect of opioids on δ receptors which inhibits adrenergic activation). Patients with poor ventricular function often rely on an elevated sympathetic tone to maintain their cardiac output and may decompensate even with pure high-dose opioid anesthesia.
  - Opioids used as sole agents may not be complete anesthetics because of an unacceptably high incidence of intraoperative awareness and hypertension.
  - The prolonged respiratory depression following the large dose opioids is also unsuitable for most non-cardiac operations.

Most clinicians always use small supplemental doses of an intravenous agent or volatile anesthetic with a primarily opioid-based anesthetic.

Muscle relaxants:

- Use muscle relaxants that have less cardiovascular effects such as vecuronium, atracurium, or cis-atracurium.
- In right ventricular failure (in which there is pulmonary hypertension), avoid muscle relaxants that produce histamine release such as atracurium which produces pulmonary vasoconstriction, with subsequent increased pulmonary hypertension and more right ventricular failure.
- Avoid pancuronium as it causes more sympathetic stimulation and increases tachyarrhythmias which are already high in patients with heart failure.

Maintenance:

In patients with heart failure, the ejection fraction is usually < 40%; therefore, **opioid-based anesthesia is recommended** with precautions (see above).

- **Volatile agents** are used **cautiously and in small doses** because:
  - they cause dose dependent myocardial depression (i.e., negative inotropic effect).
  - they cause a greater myocardial depressant effect in the failing heart than in the normal heart (i.e., the failing heart is more sensitive to the depressant effect of anesthetics than the normal heart).
- **Small doses of ketamine** can be used with the opioids.
- **N_2O and benzodiazepines** should be **avoided** in patients receiving high dose opioids as they produce severe myocardial depression with large doses of opioids.

Mechanical Ventilation:

- It decreases pulmonary congestion in left ventricular failure and improves oxygenation although it increases the pulmonary vascular resistance.
- **Avoid hyperventilation** because it may produce hypocapnia which in turn leads to secondary hypokalemia. The latter increases digitalis toxicity if it has been used.

Intraoperative Fluid Management:

It should be **done very carefully** by **pulmonary artery catheter monitoring** (if possible) to optimize left ventricular filling pressure.

Intraoperative Complications:

Acute heart failure either with normal, elevated, or low blood pressure may occur intraoperatively which necessitates management by inotropes, inodilators, or vasodilators as discussed before.

N.B.: Calcium should be avoided as an inotrope because it may precipitate digitalis toxicity (if it was used).

Postoperative Management and Intensive Care Considerations:

In intensive care unit for:

- O_2 supplementation.
- Prophylactic **ventilatory** support for 24-48 hours.
- Postoperative **pain control**.
- Continue cardiovascular support and heart failure management till the patient is hemodynamically stable.

Shock

Definition

Shock is a state of circulatory failure leading to inadequate vital organ perfusion and O_2 delivery.

Causes

A. Hypovolemic Shock:

1- Loss of **blood** (hemorrhagic shock) (intravascular volume deficit).
- External hemorrhage e.g., trauma, surgery, or gastrointestinal bleeding.
- Internal hemorrhage e.g., hematoma, hemothorax or hemoperitonium.

2- Loss of **plasma** e.g., burn or exofoliative dermatitis.

3- Loss of **fluid** and electrolytes.
- External: e.g., vomiting, diarrhea, fistulas, excessive sweating, exposed surgical wound, or hyperosmolar states (diabetic ketoacidosis, hyperosmolar nonketotic coma).
- Internal (3rd space) e.g., pancreatitis, ascites, or bowel obstruction.

B. Cardiogenic Shock (Pump Failure):

Due to loss of the ability of the heart to function as a pump.

1. **Dysrhythmias:** brady- or tachyarrhythmias.
2. **Pump failure:** myocardial **infarction**, **myocarditis**, or **cardiomyopathy.**
3. Acute **valvular** dysfunction: especially regurgitant lesions.
4. **Rupture** of the ventricular septum or the free ventricular wall.
5. **Acidosis.**
6. **Excessive drugs** such as anesthetic drugs, beta-blockers, or calcium channel blockers.

C. Obstructive Shock (Cardiac Compressive Shock):

Due to compression of the great veins and cardiac chambers, restricting their normal filling and emptying.

1. **Tension pneumothorax.**
2. **High positive end-expiratory pressure** (high PEEP) during mechanical ventilation.

Both 1 and 2 increase intrathoracic pressure which collapses the superior and inferior venae cavae and reduces the transmural pressure gradient, thereby decreasing cardiac filling.

3. Pericardial disease (**tamponade or constriction**).
4. Cardiac tumor (**atrial myxoma**).
5. Left atrial **mural thrombus.**
6. **Obstructive valvular** diseases such as aortic or mitral stenosis.
7. Disease of **the pulmonary** vasculature (massive **pulmonary embolism** or pulmonary hypertension).

N.B.: Some authors include both cardiogenic shock and cardiac compressive shock in one type called **cardiac shock.**

D. Hyperdynamic Shock (Vasogenic, Low Resistance or Distributive) Shock:

Due to venous pooling of the blood.

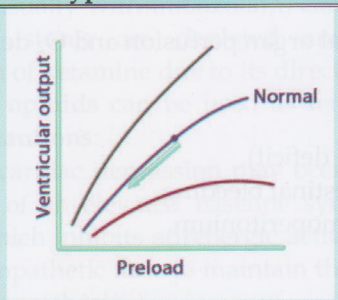
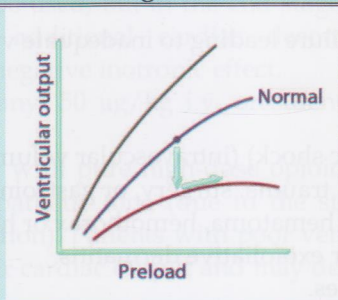
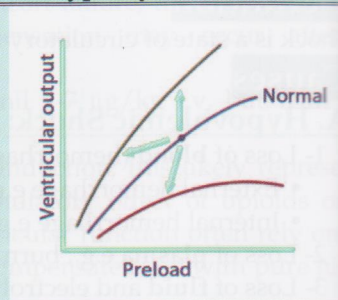
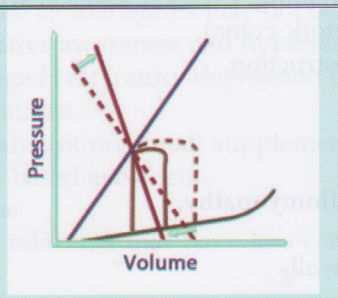
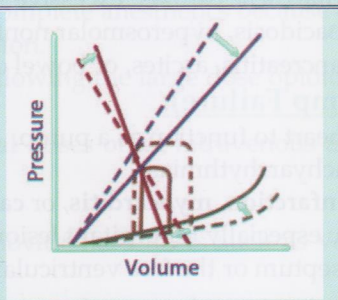
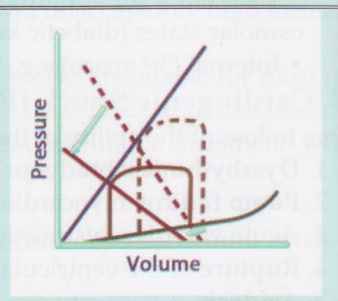
1. **Septic** shock.
2. **Anaphylactic** shock.
3. **Neurogenic** shock such as
   - brain stem dysfunction,
   - intrathecal or epidural regional anesthesia,
   - autonomic blocking drugs.

   or
   - spinal cord injury; above T6 causes severe shock and bradycardia, below T6 causes shock and tachycardia.
4. **Vasodilator drugs** such as excessive anesthetic drugs or antihypertensive drugs.
5. **Acute adrenal insufficiency.**

N.B.: Distributive shock describes the redistribution of intravascular volume to the interstitial and intracellular spaces causing decreased preload due to altered capillary permeability. It is included in the hyperdynamic shock group.

Q: What is the management of non-hemorrhagic shock?
A: All causes of shock except loss of blood causes should be discussed.

Pathophysiology of Shock

	Hypovolemic Shock	Cardiogenic Shock	Hyperdynamic Shock
Starling curves (figure 13-29)			
Pressure-Volume Loops (figure 13-30) … Normal – Pathology			
1ry Defect	**Decreased blood volume** (preload) as detected in both the starling curve and pressure volume loops (figure 13-29 and 13-30).	**Decreased contractility** (associated with increased preload) as detected in both the Starling curves (i.e., increased central venous pressure) and pressure-volume loops (i.e., increased end-diastolic pressure and pulmonary capillary wedge pressure).	**Decreased systemic vascular resistance** (associated with decreased preload) due to vasodilatation and increased capillary permeability.
Compensatory mechanisms	**Increased systemic vascular resistance** as detected in the pressure volume loops only. N.B.: The stroke volume is decreased. It can also be detected in the pressure volume loops only (not in the Starling curves).	**Increased systemic vascular resistance** as detected in the pressure-volume loops only. There is diastolic dysfunction i.e., decreased compliance detected only in the pressure-volume loops. The decreased compliance appears as a decrease in end-diastolic volume and an increase in end-diastolic pressure. N.B.: The stroke volume is decreased as detected in the pressure-volume loops only.	**Ventricular contractility and stroke volume** are variable. It is detected better in the pressure volume loops.
It is clear that pressure-volume loops are more useful than the Starling curves in understanding the pathophysiology of shock. In the decompensation stage, all parameters such as preload, afterload (systemic vascular resistance), and contractility) are decreased in the terminal stages of all types of shock.			

Assessment of Shock

Shock can be assessed by monitoring of **tissue perfusion, central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, cardiac output, and O_2 delivery**. These measurements are discussed in details in the chapter of "Monitoring during Anesthesia & Intensive Care".

Guide Lines for Treatment of Shock

1- Patient Resuscitation: is the first line of management which should be applied in emergency and critical situations. It includes Airway, Breathing, and Circulation resuscitations.

2- Treatment of the Cause: such as • controlling blood loss in hypovolemic shock,
• antibiotics in septic shock,
• anti-allergic medications in anaphylactic shock,
or • anti-ischemic medications in cardiogenic shock.

3- Management of the Primary Defect: (figure 13-31)
Administer a fluid volume challenge (500-1000 mL normal saline or 300 mL colloids) that is infused over 30 minutes, if there is no response, assess central venous pressure (CVP).

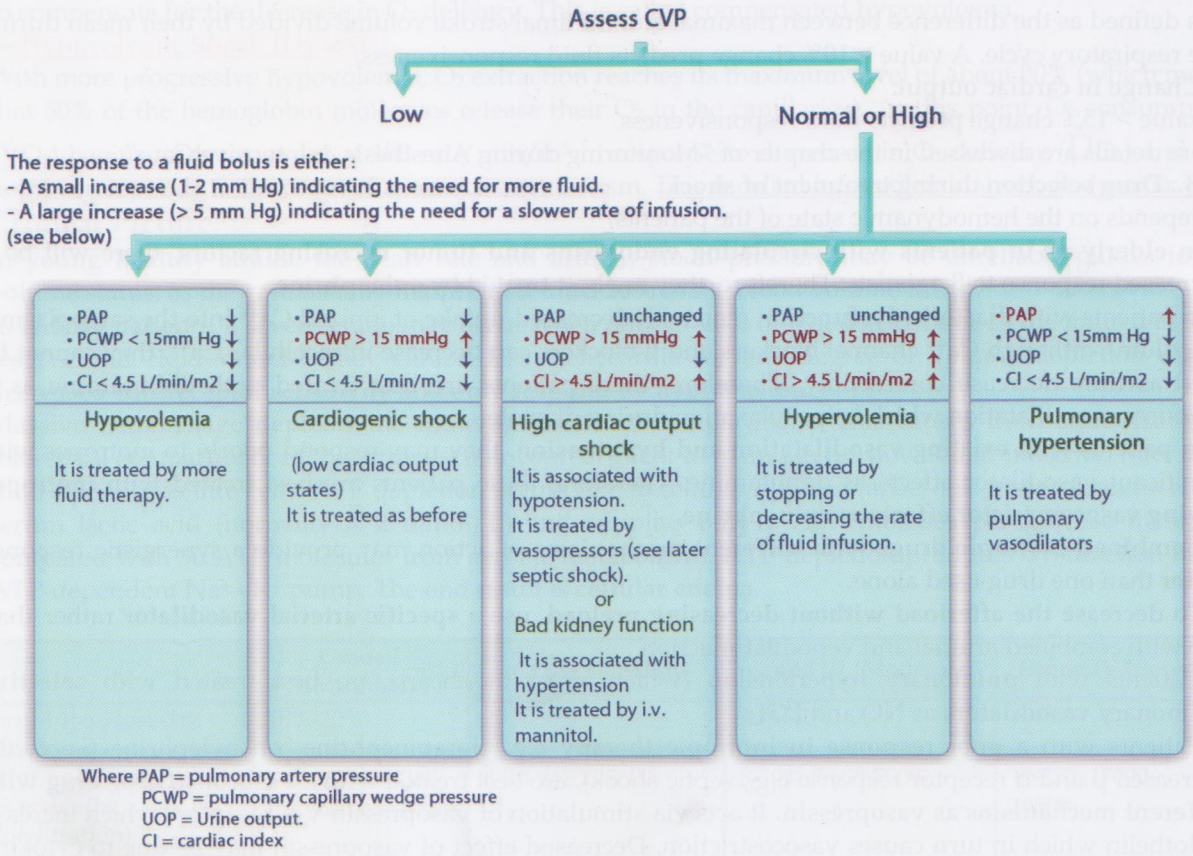


Figure 13-31: Co-monitor for reaching the diagnosis of shock

4- Treatment of Complications such as acute respiratory distress syndrome (ARDS), disseminated coagulopathy (DIC), or renal failure.

Assessment of Fluid Responsiveness in a Patient with Hypovolemic Shock:

A) Induce a Change in Cardiac Preload:

1- Acute change: administer a fluid bolus.

2- Functional change:

In mechanically ventilated patients: use existing respiratory variations in hemodynamic signals as follows:

• In mechanically ventilated patients, this functional change in preload is already occurring as a result of mechanical ventilation-induced changes in cardiac preload and can be monitored by observing the magnitude of change in hemodynamic signals in relation to cyclic changes in airway pressure.

• Arterial blood pressure rises during inspiration and falls during expiration as a result of changes in intrathoracic pressure secondary to positive pressure ventilation. In patients with preload reserve, mechanical ventilation will result in greater cyclic changes in the right ventricular and subsequently left ventricular stroke volume; therefore, can predict volume responsiveness.

In spontaneously breathing patients: use "passive leg-raising" test as follows:

• It consists of lifting the legs passively 45 degrees from the horizontal (supine) position (or tilting the bed to the same extent) and observing the change occurring in hemodynamic effects (change in stroke volume, cardiac output, or arterial pulse pressure) as a result of the gravitional transfer of blood from the lower extremities toward the intrathoracic compartment.

B) Observe the Change:

1- **Change in arterial pulse pressure:**

• **Delta pulse pressure:** difference between maximal and minimal pulse pressure during one respiratory cycle divided by their mean. A value of 13% or higher predicts fluid responsiveness.

• **Delta down:** systolic blood pressure at the end of a 5-second respiratory pause and its minimal value during the course of one mechanical breath. A value of 5 mm Hg or higher predicts fluid responsiveness.

2- Stroke volume variation:

It is defined as the difference between maximal and minimal stroke volume divided by their mean during one respiratory cycle. A value > 10% change predicts fluid responsiveness.

3- Change in cardiac output:

A value > 15% change predicts fluid responsiveness.

More details are discussed in the chapter of "Monitoring during Anesthesia & Intensive Care".

N.B.: Drug selection during treatment of shock:

It depends on the hemodynamic state of the patients:

• In **elderly or in patients with circulating endotoxins and tumor necrosing factors**, there will be a decreased response to β agonists. Therefore, they are best treated by **epinephrine.**

• In patients with **diastolic dysfunction** (i.e., with decreased uptake of ionized Ca^{++} into the sarcoplasmic reticulum), although Ca^{++} channel blockers and β blockers can decrease intracellular Ca^{++}, they cannot be used as they decrease contractility. Therefore, these patients are best treated with **dobutamine** as it produces vasodilatation which helps relaxation during diastole.

• In patients with **existing vasodilatation and hypotension,** they may respond poorly to inotropes with significant vasodilator effects as dobutamine. Therefore, these patients are best treated with **inotropes having vasoconstrictor effects as epinephrine.**

• **Combined inotropic drugs with different mechanisms** of action may provide a synergistic response **better** than one drug used alone.

• **To decrease the afterload without decreasing preload,** use a **specific arterial vasodilator** rather than one with combined arterial and venodilator action.

• Patients with **pulmonary hypertension** (which affect the heart) are best treated with **selective pulmonary vasodilators** as NO and PGI_2.

• Patients with a **poor response to inotropic therapy** e.g., norepinephrine, phenylephrine (i.e., with decreased β and α receptor response e.g., septic shock), are best treated with a **vasoconstrictor drug with different mechanisms as vasopressin.** It acts via stimulation of vasopressin V_{1A} receptors which increase endothelin which in turn causes vasocostriction. Decreased effect of vasopressin may be due to cytokine induced down-regulation of V_{1A} receptors.

Treatment of Shock in Children

The same pathophysiology and management of shock as in adults with the following notes:

Augmentation of the cardiac output (cardiac output = heart rate x stroke volume) is very important:

a) Heart Rate: Heart rate **must be increased** by:

• Vagolytic drugs as atropine.

• Positive chronotropic drugs as isoproterenol or epinephrine because:

1. Up to 5 months age, cardiac output is dependent on the heart rate more than the stroke volume.
2. Up to 50% increase in the heart rate above control values is well tolerated in children and can increase cardiac output.

b) Stroke Volume: must be increased by:

• **Increasing the preload** by fluid.

• **Increasing contractility**.

• **Decreasing the afterload.**

Hypovolemic Shock and Hypovolemia

Definition and Causes: are discussed above.

Compensatory Mechanisms:

The compensatory mechanisms during hypotension and shock are discussed before with the control of arterial blood pressure. They include:

a- Immediate control: sympathetic stimulation and baroreceptor reflex.

b- Intermediate control: Renin-angiotensin-aldosterone system.
Arginine vasopressin.
Alteration in capillary fluid exchange.

c- Long term control by the kidneys: sodium and water retention.

Pathophysiology of Hypovolemia and O_2 Transport:

a- Compensated Hypovolemia:

In early stages of hypovolemia, there is a decline in systemic O_2 delivery ($\dot{D}O_2$), but systemic O_2 uptake ($\dot{V}O_2$) remains unchanged i.e., > 100 mL/min/m² due to an increase in O_2 extraction from capillary blood to compensate for the decrease in O_2 delivery. This is called compensated hypovolemia.

b- Hypovolemic Shock (Dysoxia):

With more progressive hypovolemia, O_2 extraction reaches its maximum level of about 50% (which means that 50% of the hemoglobin molecules release their O_2 in the capillaries). At this point, O_2 consumption ($\dot{V}O_2$) begins to decrease i.e., < 100 mL/min/m² in response to decreases in O_2 delivery ($\dot{D}O_2$) and this point corresponds to the onset of anaerobic metabolism. This is called hypovolemic shock or dysoxia.

Clinical Picture:

In **young healthy adults**, the heart rate and arterial blood pressure may be unreliable guides to the volume status, as they are usually **maintained until 20%** of the blood volume is lost.

In **elderly patients**, a severe grade may occur when only 15-20% of blood is lost due to the limited cardiac reserve and rigid vessels. They exhibit less tachycardia for any degree of volume depletion due to decreased baroreceptor sensitivity and **only respond by hypotension.**

Massive hemorrhage depletes the intravascular fluid compartment. This causes fluid shifts from the interstitial compartment to the intravascular compartment to maintain cardiovascular integrity. Interstitial fluid also moves into cells. ATP depletion occurs due to cellular hypoxia (anaerobic metabolism increases serum lactic acid (normally < 2 mmol/L) and supplies only 2 ATP moieties per glucose molecule, compared with 36 ATP molecules from aerobic metabolism). ATP depletion produces dysfunction of the ATP-dependent Na^+ - K^+ pump. The end result is **cellular edema**.

	Grade I (Minimal)	Grade II (Mild)	Grade III (Moderate)	Grade IV (Severe)
% of blood lost (in shock) or **% of body weight lost as water (in dehydration)** 1% loss equals loss of 700 mL in a 70 kg body weight person	10%-20% 4-6% (2800-4200 mL lost)	20%-30% 6-8% (4200-5600)	30%-40% 8-10% (5600-7000)	> 40% 10-15% (7000-10500)
Pathophysiology	• Minimal change	• Decreased peripheral perfusion only of organs able to withstand prolonged ischemia (skin, fat, muscle and bone). • Arterial pH is normal.	• Decreased central perfusion of organs able to tolerate only brief ischemia (liver, gut, and kidney). • Metabolic acidosis.	• Decreased perfusion of the heart and brain. • Severe metabolic acidosis + respiratory acidosis may occur.
Clinical picture • Heart rate (beat/min)	• Normal	• 100-120	• 120-140 (thready pulse)	• > 140 (thready pulse) In pre-terminal cases, bradycardia may occur

• Blood pressure (mm Hg)	• Normal	• Orthostatic hypotension	• Systolic < 100 with supine hypotension	• Systolic < 80
• Urine output (mL/min)	• Normal (1 mL/kg/hr)	• 20-30 mL (< 0.5 mL/kg/hr)	• 10-20 mL	• Nil
• Sensorium	• Normal	• Normal with nausea and apathy	• Restlessness	• Impaired consciousness, coma and finally death
• Peripheral circulation	• Normal and may be sweating	• Cold, pale, dry axilla and groin	• Cold, pale and slow capillary refilling	• Cold, clammy with peripheral cyanosis
• Mucous membrane (tongue)	• Dry tongue (and thirst)	• Very dry	• Very dry	• Parched
• CVP (cm H_2O), manubrium is zero reference	• Normal	• (-3) collapsed neck vein	• (-5)	• (-8)
• Sunken eye in dehydration only	• +	• ++	• +++	• ++++
• Skin turgor (elasticity) in dehydration only	• ↓	• ↓↓	• ↓↓↓	• ↓↓↓↓

N.B.: **Orthostatic hypotension** is defined as a decline of blood pressure > 10 mm Hg and an increase in heart rate > 30 beat/min that do not return to normal within several minutes.

Normally, transition from the supine to the sitting position will decrease blood pressure by less than 10 mm Hg and increase heart rate by less than 10 beat/min in a healthy person as this change in position causes a shift of 7-8 mL/kg of blood to the lower extremities.

N.B.: **Skin turgor (elasticity)** is difficult to be assessed in elderly (in whom natural loss of subcutaneous tissue elasticity occurs) giving a false impression of decreased skin turgor. The most reliable sites are the anterior thigh, forehead, sternum, clavicle, and tibia.

N.B.: **Sunken eyes and decreased skin turgor** need time to occur; therefore, they are common with dehydration (i.e., a subacute condition) rather than with hypovolemic shock (i.e., an acute condition).

N.B.: The term "dehydration" should not used as a substitute for hypovolemia because the term "dehydration" is reserved to mean insufficient water relative to total body solute, while the term "hypovolemia" means decreased effective intravascular volume.

Investigations: are mainly to determine the cause of hypovolemia.

1- The hematocrit (Hct): in hypovolemic shock, hematocrit may be one of the following:

a- Normal hematocrit: It occurs when blood loss occurs rapidly (i.e., **acute blood loss**) where there is loss of whole blood with proportional decreases in the volume of plasma and erythrocytes; therefore, **the use of hematocrit** to estimate acute blood loss **is unreliable and inappropriate**.

b- Low hematocrit: It occurs when either:

- **The patient has bled slowly and recognition of bleeding is delayed. In absence of volume resuscitation**, the hematocrit will eventually decrease because hypovolemia activates the renin-angiotensin-aldosterone system leading to Na^+ and water retention. This process begins **8-12 hours after acute blood loss and can take a few days to become fully established**.

or • **The patient has bled and fluid resuscitation has been instituted**.

c- High hematocrit: it occurs when either:

- Hypovolemia results from loss of non-sanguineous fluid e.g., emesis or diarrhea i.e., dehydration (hemoconcentration).

or • Resuscitation of acute blood loss is performed by packed red blood cells without other fluid resuscitation.

Hematocrit can assess allowable (estimated) blood loss i.e., **trigger point for blood transfusion.**

$$\text{Estimated blood loss} = \frac{\text{Preoperative Hct} \quad \text{Hct } 30\%}{\text{Preoperative Hct}} \times \text{blood volume}$$

2- Arterial (Serum) Lactic Acid:

Serum lactic acid is elevated in shock indicating tissue hypoxia. The rate at which arterial lactic acid is cleared indicates efficacy of fluid resuscitation (**i.e., used as a marker of the presence of ischemia and its resolution**). Failure to clear elevated lactic acid is an indication of inadequate resuscitation or presence of other undiagnosed causes of hypoperfusion.

3- Arterial Blood Gases: show metabolic acidosis.

- **Decreased s. bicarbonate**.

• **Base deficit**: like arterial lactic acid, it is a marker of global tissue acidosis from impaired oxygenation. It indicates only metabolic acidosis without any respiratory effect. Its magnitude indicates the severity of blood loss and it should resolve with adequate resuscitation.

4- Renal Function Tests:

Decreased renal blood flow causes:

• Increased serum blood urea nitrogen (BUN) out of proportion to increased serum creatinine (increased BUN: creatinine ratio) (i.e., prerenal uremia) often greater than 30:1 due to increase BUN reabsorption more than creatinine.

• Stimulation of ADH and aldosterone which causes low-volume concentrated urine with:

▫ Decreased urinary Na^+ concentration < 10-20 mmol/L (due to increased Na^+ reabsorption by aldosterone).

N.B.: Hypovolemia due to osmotic diuresis or excessive administration of mannitol or diuretics is associated with increased urine volume with increased urine Na^+.

▫ Increased K^+ and H^+ excretion in the urine (due to the action of aldosterone).

▫ Increased urinary specific gravity > 1.010.

▫ Increased urinary Osmolality > 450 mOsmol/kg.

N.B.: During anesthesia, besides the other clinical pictures, capnography shows a decrease in end-tidal CO_2 due to a decrease in blood flow to the lungs. There is also a widening of the arterial-end-tidal CO_2 gradient, when capnography is compared to arterial blood gases.

5- Hemodynamic Monitors: such as

• Central venous pressure monitoring.

• Pulmonary artery pressure and pulmonary capillary wedge pressure monitoring.

• Transesophageal echocardiography.

More details are discussed in the chapter of "Monitoring during Anesthesia & Intensive Care".

Treatment of Hypovolemic Shock:

1- Patient Resuscitation: is the first line of management which should be applied in emergency and critical situation. It includes **A**irway, **B**reathing, and **C**irculation resuscitations.

• **Peripheral cannulas**: multiple large bore (14-16 gauge) cannulas should be inserted.

• **Central venous line:** Although it may provide useful information regarding the volume status, it has the following disadvantages: - It is time-consuming.
- It may produce life threatening complications e.g., pneumothorax.
- The triple-lumen catheters have usually a relatively small lumen.

It can be introduced later.

• **Trendelenburg position (supine and legs up):** Although this position can elevate mean arterial blood pressure, some authors have showed that it does not promote venous return or increase cardiac output due to the high capacitance (distensibility) of the venous circulation.

• **Pneumatic anti-shock garments** (Military anti-shock trousers): They are used to decrease bleeding in lower extremities and abdomen and increase systemic vascular resistance. It acts as thoracic aortic cross clamping; therefore, it helps perfusion of the heart and brain. Bleeding wounds above the level of the suite (e.g. thorax or head) contraindicate the use of these garments because of the risk of increasing hemorrhage. It is only deflated when fluid volume is given (figure 13-32).

Gradual deflation is essential to avoid marked hypotension and metabolic acidosis produced by reperfusion of ischemic tissues.



Figure 13-32: Pneumatic anti-shock garment

2- Treatment of the Cause: Search for the source of bleeding or fluid loss and it should be managed e.g., direct pressure over the site of external bleeding until definitive surgical control can be secured (tourniquets can cause reperfusion injuries).

3- Fluid Therapy:

All fluids should be warmed. The type of the fluid depends mainly on the availability.

1- Blood:

• **Fully cross-matched whole blood** is ideal (typing, cross-matching, and indirect coomb's test take 45-60 min), but in emergency situations, **type specific blood** with an abbreviated cross-matched test (takes 5-10 min) is enough although it may cause an antibody reaction in less than 1% in males and 2% in parous females.

• **Uncrossed O negative packed red blood cells** should only be given in life-threatening blood loss that can not be adequately replaced by the blood of the same group of the patient. It should not be used alone; it should be used with other fluids.

• Complication of massive blood transfusion is discussed in chapter of "Fluid & Electrolyte Disturbances".

2- Crystalloid solutions:

Advantages:

- They can correct interstitial and intravascular fluid losses.
- They decrease blood viscosity which may enhance perfusion.
- They are readily available and economically effective.

Disadvantages:

- They are distributed between the intravascular space (25%) and the interstitial space (75%) according to their original sizes within 20-30 minutes of infusion; therefore, large amounts of crystalloids (3-4 parts) are needed to compensate for the loss of one part of blood and so they may cause both pulmonary and peripheral edema i.e., if 1000 mL of normal saline is given, only 250 mL will remain in the intravascular space; therefore, blood loss should be compensated by 3-4 times volume of crystalloids.

Types: Only the crystalloids where the main components is Na^+ can be used because Na^+ will not be allowed to enter into cells (due to presence of Na^+-K^+ ATPase pump), unlike glucose containing solutions where the glucose enters cells and then becomes metabolized and the water volume will be distributed according to the original volume of spaces i.e., 1000 mL of glucose infusion will be distributed as follows; 666 mL intracellularly, 333 mL extracellularly (250 mL in the interstitial spaces and only 83 mL remains intravascularly).

• **Normal saline:** is suitable for extracellular deficit especially interstitial fluid replacement, but it causes hyperchloremic metabolic acidosis.

• **Lactated ringer's injection**: is less likely to cause hyperchloremic acidosis than normal saline, but its Ca^{++} content is less compatible with blood transfusion as the Ca^{++} may combine with the citrate content (an anticoagulant in the blood transfusion bags). Lactated ringer's solution can treat patient's acidosis because lactate is metabolized in the liver to bicarbonate.

• **Ringer acetate solution**: can also treat patient's acidosis because the acetate is metabolized in the muscle to bicarbonate.

• **Hypertonic solution** (small volume resuscitators) such as:

7.5% saline (its osmolarity is 2400 mOsmol/L),
or 3.0% saline (its osmolarity is 1026 mOsmol/L).

Uses: It has a role during emergency resuscitation especially in:
- a pre-hospital setting and in resuscitation of battlefield casualties,
- and patients that cannot tolerate edema formation e.g., closed head injury.

Actions:
- This small volume with high osmolarity **draws fluid** into the vascular compartment resulting in expanding plasma volume (every 1 mL of hypertonic saline increases plasma volume 3 mL).
- It increases the preload and decreases the afterload by its **vasodilatory effect** resulting in increased ejection fraction i.e., an inotropic action.

Side effects:
- **Vasodilatation** and hypotension.
- **Thrombophlebitis;** so, it should be given in a central line only.
- Mild to moderate **dilutional hypokalemia**.
- **Hyperchloremic hypernatremia** (it should be stopped if s. Na^+ reaches > 160 mmol/L). It may cause acidosis due to increased renal HCO_3^- loss secondary to increased s. Cl^-.

- **Cellular dehydration** which is useful in closed head injury.
- Rapid i.v. infusion may cause **central pontine myelinolysis** (characterized by dysarthria, dysphagia, quadri-, or paraparesis).
- Suppression of neutrophil function.

N.B.: Dextrose containing solutions should be avoided because they may increase ischemic brain damage. They are only given if there is documented hypoglycemia.

3- Colloid solutions:

80% of the infused colloids remain in the intravascular compartment for longer periods (due to their large molecular weight) and only 20% (those with low molecular weights) escape to the interstitial fluid.

Albumin is better than dextran or starch as it does not cause coagulopathy, but with possibility of infection transmission.

The amount of fluid given: should be based on **clinical signs** (the best parameter) and central venous pressure, and **estimation of the resuscitation volume** can be performed by the following steps:

1- Estimate normal blood volume: = 66 mL/kg (males)
= 60 mL/kg (females)

2- Estimate % loss of blood volume grade I = 10%-20%
grade II = 20%-30%
grade III = 30%-40%
grade IV = > 40%

3- Calculate volume deficit: = blood volume x % loss of blood volume.

4- Determine resuscitation point: = volume deficit x 1-1.5 colloids
= volume deficit x 3-4 crystalloids

End points of resuscitation include:
- Cardiac index = 3 L/min/m^2
- Systemic O_2 delivery ($\dot{D}O_2$) = > 500 mL/min/m^2.
- Systemic O_2 uptake ($\dot{V}O_2$) = > 100 mL/min/m^2.
- Arterial lactate < 2 mmol/L or base deficit > -2 mmol/L.

4- Vasopressors:

They are not given in hypovolemic shock except if there is severe hypotension not responding to aggressive fluid therapy. Some give low dose dopamine to increase renal blood flow.

Causes of Persistent Hypotension

1- Continued blood loss (external or internal): its rate exceeding the rate of fluid replacement. Platelets and clotting factors should be checked.

2- Presence of another undiagnosed type of shock such as
- Coexisting cardiogenic shock: as tamponade or myocardial contusion.
- Coexisting obstructive shock: as pneumothorax or hemothorax.
- Coexisting distributive shock: as septic shock or neurogenic shock.

3- Coexisting metabolic problems: as acidosis (pH < 7.1), hypokalemia, or hypocalcemia.

4- Irreversible shock.

Irreversible Shock (Refractory Shock)

It occurs when the shock state persists for several hours (usually 3-5 hours). This causes irreversible shock whatever treatment, fluids, or vasopressors are given and leads to death. Some researches show that vasopressin i.v. infusion at a rate of 1-4 mUnit/kg/min is effective in treating this terminal condition.

Mechanism:

1. Alteration of Precapillary Sphincter Tone:

Early: Stimulation of sympatho-adrenal system causes vasoconstriction of pre-capillary and post-capillary sphincters resulting in a decrease in capillary perfusion which causes:
- tissue hypoxia, and
- decreased capillary pressure which in turn produces shift of fluid from the interstitial and intracellular spaces to the intravascular space.

Later: Tissue hypoperfusion produces lactic acidosis which increases H^+ ions. This causes dilatation of the pre-capillary sphincter while the post-capillary sphincter remains constricted. Therefore, stagnation and pooling of blood in the capillaries occurs resulting in:
- further tissue hypoxia, and

• increased capillary pressure which shifts fluid from the intravascular to the interstitial compartment.

2. Myocardial Depression: .

Due to: • The myocardial depressant factor produced by the pancreas (MDF).
• Sepsis.
• Acidosis.
• Cerebral ischemia causing inhibition of the vasomotor center.
• Decreased coronary blood flow due to hypotension and tachycardia.

Cardiac Dysrhythmias

Anatomy of Cardiac Pacemaker and the Conduction System

The Sino-Atrial (SA) Node	The Atrio-Ventricular (AV) Node
It is the primary site for impulse initiation, spontaneously discharging at a rate between 60-100 beats/min. It overdrives other potential pacemakers in the heart.	It conducts the impulse from the right atrium to both ventricles. It has a long refractory period (i.e., physiological delay) to help prevent over-stimulation of the ventricles by very rapid atrial impulses if occurs such as atrial fibrillation.
It is located at the junction of the superior vena cava and the right atrium.	It is located in the septal wall of the right atrium, anterior to the coronary sinus and above the insertion of the septal leaflet of the tricuspid valve.
It is innervated by sympathetic and parasympathetic nerve endings.	It is innervated by sympathetic and parasympathetic nerve endings.
It is supplied by the right coronary artery in 60% of individuals or by the left circumflex coronary artery in 40% of individuals.	It is supplied by the right coronary artery in 85% to 90% of population and from the left circumflex coronary artery in the remaining 10-15%.

• **Fibrous atrio-ventricular rings (annulus fibrosa) of the mitral and the tricuspid valves:** prevent passage of the impulses from the atria to the ventricles normally (i.e., it electrically separates the atria from ventricles) where impulses reach the ventricles only via the AV node.

• **The bundle of His** conducts the impulses from the AV node down the conduction tract. The bundle of His quickly divides into - the right bundle branch,
and - the left bundle branch which further divides into the left anterior superior fascicle and the left posterior inferior fascicle.

Mechanisms of Dysrhythmias

Two electro-physiological bases are involved:

A. Abnormality in Impulse Formation (Abnormality in Automaticity)

• In the normal heart, the SA node functions as the pacemaker of the heart by undergoing spontaneous phase 4 depolarization (i.e., has automaticity) and overdrives other potential pacemakers in the heart.
If the SA node does not fire, other slower pacemaker cells will usually take over pacemaker function.
The SA node usually fires at a rate 60-100 times/min (which overrides other cells).
Cells near the AV node, the so-called junctional pacemaker, fire at 40-60 times/min.
Ventricular pacemaker cells (and ventricular muscle cells) fire at a rate 30-45 times/min.

• Increased slope of spontaneous phase 4 depolarization (of the SA node) causes enhancement of automaticity which in turn produces tachycardia and ventricular irritability leading to tachyarrhythmias.

• Decreased slope of spontaneous phase 4 depolarization (of the SA node) decreases enhancement of automaticity of the SA node, but increases enhancement of automaticity of lower pacemakers (or even any cell in the heart) leading to bradyarrhythmias.

Afterdepolarizations and Triggered Dysrhythmias

Definition: After-depolarizations are oscillations in membrane potential that occur during or after repolarization under special circumstances such as digitalis toxicity or other cardiac diseases i.e., it occurs **during diastole** and mimics phase "4" depolarization. These after-depolarizations can reach a threshold causing trigger sustained repetitive firing and lead to a complete depolarization (i.e., a secondary depolarization). Once triggered, the process may be self-sustaining and results in triggered dysrhythmias.
The after-depolarizations are either:

- Early after-depolarizations (in phase 2 and 3): They are associated with triggered dysrhythmias that are enhanced by slow heart rates and are treated by accelerating the heart rate with pacing or with positive chronotropic drugs.
- Delayed after-depolarizations (after phase 3): They are associated with triggered dysrhythmias that are enhanced by fast heart rates and can be treated with negative chronotropic drugs.

B. Abnormality in Impulse Conduction (Reentry Pathway, Reentry Excitation or Unidirectional Block)

It causes most of the **tachyarrhythmias** and **premature beats.**

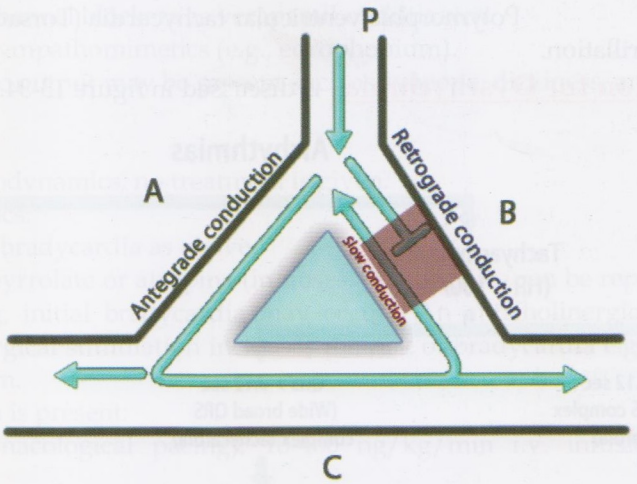
For sustained reentry occurrence, there must be special circumstances which include:

1- Two limbs (limb "A" and "B") in the myocardium that **differ in conductivity or refractoriness** and can form **a closed electrical circuit** (figure 13-33).

2- The **limb "A" should have antegrade conduction** e.g., the AV node

3- The **limb "B" should have unidirectional block** e.g., due to a functional cause, scar tissue, or presence of a bypass tract that allows direction of impulses in **a retrograde conduction only**. The conduction in limb "B" should be slow or the limb "B" should be of a sufficient length to allow arrival of the impulse to limb "A" after its recovery from the refractory period. Therefore, a circus movement and sustained conduction occur resulting in tachyarrhythmias.

N.B.: Very rarely, circus movement occurs in an opposite direction i.e., **antegrade conduction via the bypass accessory tract** e.g., a bundle of Kent and **retrograde conduction via the AV node**. This causes an abnormal QRS complex shape with a delta wave; therefore, it can be mistaken with ventricular tachycardia.



P = Purkinje fiber dividing into 2 limbs.
A = Normal limb with antegrade conduction.
B = Abnormal limb with retrograde (unidirectional) conduction.
C = Ventricular muscle cell.

Figure 13-33: Re-entry pathway

Factors initiating reentry excitation:
- Hypoxemia.
- Acidosis.
- Myocardial ischemia.
- Hypercarbia.
- Digitalis.

N.B.: Some authors recommend the term "dysrhythmia" instead of "arrhythmia" because dys- = irregular, but a- = no.

Hemodynamic Effects of Dysrhythmias

1. Effect of brady-dysrhythmias:

It causes a serious **decrease in cardiac output** (with syncope, dizziness, angina, or heart failure) especially in pulmonary hypertension, congestive heart failure, mitral stenosis, mitral regurgitation, aortic stenosis, and constrictive pericarditis.

2. Effect of tachy-dysrhythmias:

It decreases the time of diastolic filling of ventricles especially in mitral stenosis producing a decrease in cardiac output.

It increases the tension time index and increases myocardial O_2 consumption especially in aortic valve diseases and ischemic heart diseases.

3. Effect of ventricular dysrhythmia:

It causes less efficient contractions especially in aortic stenosis, pulmonary stenosis, pulmonary hypertension and systemic hypertension.

Classification of Dysrhythmias

A) Supraventricular dysrhythmias:

1- Sinus bradycardia.
2- Sinus tachycardia.
3- Sinus (phasic or respiratory) dysrhythmia.
4- Premature atrial and premature junctional beats.
5- Atrio-ventricular rhythm (nodal rhythm).
6- Paroxysmal supraventricular tachycardia: Paroxysmal atrial tachycardia.
Atrioventricular reentrant tachycardia.
7- Wandering atrial pacemaker (multifocal atrial tachycardia).
8- Atrial flutter.
9- Atrial fibrillation.

1, 2, and 3 sometimes are called sinus rhythm while from 4 to 9 are called supraventricular dysrhythmias.

B) Ventricular dysrhythmias:

1- Premature ventricular contractions.
2- Ventricular tachycardia: Monomorphic ventricular tachycardia (with or without pulse).
Polymorphic ventricular tachycardia (Torsade de Pointes).
3- Ventricular fibrillation.

Other Classification for Dysrhythmias is discussed in figure 13-34.

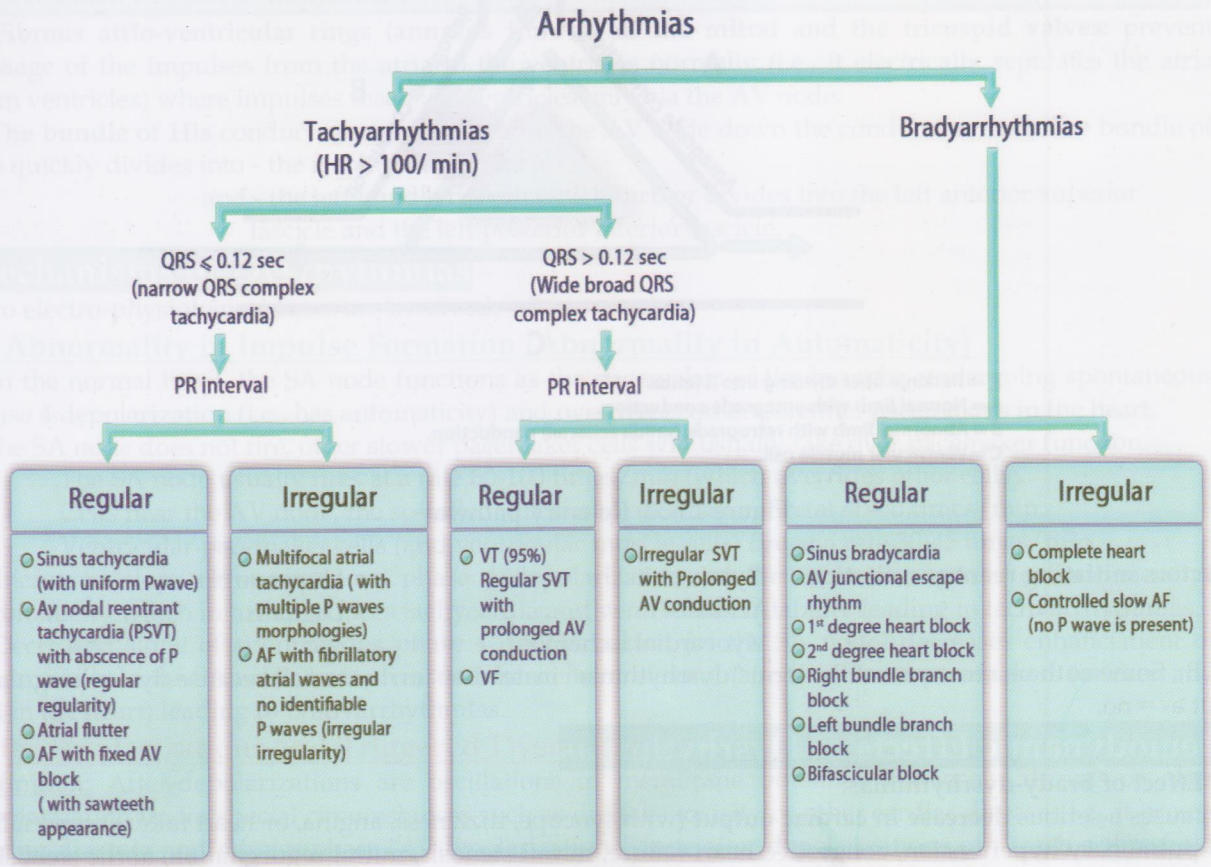


Figure 13-34: Classification of arrhythmias

All the ECG traces are present in the appendix at the end of the book.

A) Supraventricular Dysrhythmias:

1- Sinus Bradycardia:

ECG: • Sinus i.e., P wave is positive in lead II and negative in aVR.
• Each QRS complex is preceded by a P wave.
• Heart rate is < 60 beat/min.

Causes: due to decreased normal discharge of the SA node.

1. Physiological: **In athletes,** it is a normal finding.
2. Pathological: • Hypothyroidism. • Hypothermia. • Increased intracranial tension.
• Carotid sinus syndrome. • Acute hyperkalemia. • Sleep apnea syndrome.
• Sick sinus syndrome (degenerative disease in SA node in the elderly).
• After myocardial infarction (SA node disease ischemia).
3. Intraoperative onset: There is vagal stimulation such as:
• A second dose of succinylcholine. • Halothane.
• During laryngoscopy especially with a straight blade (as it touches the lower surface of the epiglottis, which is vagally innervated).
• Traction on extraocular muscles (oculo-cardiac reflex).
• Abdominal insufflation, traction on the peritoneum or mesentery.
• During high spinal or epidural anesthesia (see chapter of "Regional and Local Anesthesia").
4. Pharmacological: • Digitalis.
• Sympatholytics (e.g., β-blockers).
• Opioids (e.g., fentanyl or sufentanil).
• Ca^{++} channel blockers as verapamil or diltiazem.
• Para-sympathomimetics (e.g., edrophonium).

Clinical Picture: of low cardiac output may be present such as syncope, dizziness, angina…etc.

Treatment:

1- Treatment of the cause.
2- If it does not affect the hemodynamics, no treatment is given.
3- If it affects the hemodynamics:
• Stop drugs which cause bradycardia as above.
• Anticholinergics: glycopyrrolate or atropine (in doses > 0.5 mg i.v., can be repeated with maximum 3 mg. In doses < 0.5 mg, initial bradycardia may occur). An anticholinergic drug may be given prophylactically when surgical stimulation increases the risk of bradycardia e.g., ophthalmic surgery or 2nd dose suxamethonium.
• If refractory bradycardia is present:
▫ Isoprenaline (pharmacological pacing): 10-400 ng/kg/min i.v. infusion according to the response.
▫ Electric cardiac pacing. Epinephrine or dopamine can be used until a pacemaker is applied.
▫ Glucagon 3mg i.v bolus followed by 3 mg/hour i.v. infusion in cases of toxicity of β blockers or Ca^{++} channel blockers that is unresponsive to atropine.

2- Sinus Tachycardia:

ECG: • Sinus i.e., P wave is positive in lead II and negative in aVR.
• Each QRS complex is preceded by a P wave.
• Heart rate is > 100 beat/min up to 180.
• Gradual onset and offset, but if due to reentry mechanisms, sudden onset occurs.

Causes: due to increased normal discharge of the SA node by sympathetic stimulation.

1. Physiological: Exercise, anxiety, or pain.
2. Pathological: • Thyrotoxicosis. • Fever. • Hypovolemia.
• Acute hypokalemia. • Pulmonary embolism. • Congestive heart failure.
• Anemia. • Pericarditis. • Pericardial tamponade.
• Ethanol withdrawal. • Acute myocardial infarction/ischemia.
3. Intraoperative onset: • Light anesthesia. • Hypoxemia.
• Hypercarbia. • Acidosis.
• Hypoglycemia. • Malignant hyperthermia.
• Incompatible blood transfusion.
4. Pharmacological: • Sympathomimetics: epinephrine, ephedrine, or isoprenaline.

- Para-sympatholytics: atropine or glycopyrrolate.
- Caffeine, nicotine, cocaine, or amphetamine.

Clinical Picture: palpitations and awareness of heart beats.

Treatment:

1- Treatment of the cause.

2- If it is associated with hemodynamic effects especially myocardial ischemia, β blockers as i.v. esmolol or propranolol should be given.

Q: What are the causes of intraoperative bradycardia and tachycardia?

A: All the causes of bradycardia and tachycardia should be discussed including the physiological, pathological, intraoperative onset and pharmacological causes.

3- Sinus (Phasic, Respiratory) Dysrhythmias:

ECG: • Sinus rhythm with an irregular rate with respiration where:
During inspiration a slight increase in the heart rate occurs due to a decrease in vagal tone, and during expiration a slight decrease in the heart rate occurs due to an increase in vagal tone.

Cause: It is a normal physiological state where variations of intrathoracic pressure during inspiration and expiration cause changes in heart rate. This is called **Bain-bridge reflex.** It is common in children and young people, but tends to decrease with age.

Treatment: No need for treatment.

N.B.: Sick Sinus Syndrome:

ECG: It needs 24 hours Holter ECG to make a diagnosis. Sick sinus syndrome may be presented with one of the following pictures:

- Unexpected persistent severe bradycardia (the most common form).
- Episodes of sinus arrest.
- Paroxysmal supraventricular tachycardia from ectopic foci when the SA node is not working; therefore, it is sometimes called **tachy-brady syndrome**.
- Paroxysmal or chronic atrial flutter or atrial fibrillation.
- Slow return to sinus rhythm after cardioversion.
- Lack of increased sinus rate > 90 beat/min after i.v. 1.5-2 mg atropine.

Cause: Irreversible SA node dysfunction occurs which is characterized by intrinsic inadequacy of the SA node in performing its pacemaker function due to automaticity dysfunction or failure of the SA node impulse to activate the rest of the atrium.

Treatment:

1- Pacemaker insertion: Patients suspected to have sick sinus syndrome should be investigated before any elective surgery is done, and a decision is made whether temporary or permanent cardiac pacing is necessary. **Sick sinus syndrome is the cause of 50% of pacemaker insertion.** Indications of pacemakers in sick sinus syndrome:

- Severe symptoms.
- Presence of supraventricular tachycardia. A temporary pacemaker should be placed before the usage of drugs which treat supraventricular tachycardia e.g., digoxin, verapamil, or β blockers, otherwise severe bradycardia may occur.

2- Long-term anticoagulants (by some authors).

4- Premature Atrial and Premature Junctional Beats:

ECG: • The beat is premature i.e., earlier than expected.
- Abnormal shaped P wave or fused with the T wave of the preceding beat.
- QRS complex is normal due to activation of the ventricles via the normal conduction pathway.

Unlike premature ventricular contractions, premature atrial contractions are not followed by a pause.

Cause: It arises from an ectopic pacemaker in the atrium or near the AV node. It is precipitated by sympathetic stimulation.

1- Normally in persons with increased emotions or who drink excessive coffee.

2- Sympathomimetic drugs.

3- Hyperthyroidism.

Clinical Picture: Awareness of a fluttering or a heavy heart beat.

Treatment:

Increase the HR by i.v. atropine that usually abolishes them.

5- Atrio-Ventricular (AV) Junctional Rhythm (Nodal Rhythm):

ECG: • If heart rate is 40-60 beat/min, it is called AV junctional escape rhythm.
If heart rate is 100-250 beat/min, it is called AV junctional tachycardia.
• The P wave is retrograde i.e., negative in L II and positive in aVR (i.e., atrial depolarization occurs in the opposite direction) or the P wave is hidden in the QRS complex (i.e., atrial depolarization occurs in the same time of ventricular depolarization).

Cause: There is a continuous rhythm of a pacemaker which arises from the AV node or nearby tissues. It usually occurs with **halothane anesthesia**, myocarditis, myocardial ischemia, digitalis toxicity.

Clinical Picture: It may cause loss of atrial kick leading to a fall in cardiac output with syncope, dizziness, angina….etc.

Treatment:

1- Treatment of the cause e.g., decrease halothane concentration or change to another volatile agent.
2- Atropine or glycopyrrolate i.v. if associated with significant hemodynamic changes.

6- Paroxysmal Supraventricular Tachycardia (PSVT):

ECG: • Sudden onset and sudden offset of at least 3 or more consecutive premature supraventricular beats, either non-sustained (i.e., ≤ 30 sec) or sustained (> 30 sec).
• Heart rate is 100-250 beat/min and very regular (unlike sinus tachycardia as the heart rate reaches 100-189 beat/min and shows beat to beat variability).
• It occurs in paroxysms.

Types:

a. Paroxysmal Atrial Tachycardia:

ECG: As above in addition to: • P wave is different than normal.
• QRS complex: is normal.

Cause: There is a rapidly firing ectopic focus in the atrium especially with Wolf-Parkinson-White syndrome or other pre-excitation syndromes.

b. AV Nodal Reentrant Tachycardia: (the most common type of PSVT)

ECG: As above in addition to: • P wave is hidden in the QRS complex i.e., both atria and ventricles are activated simultaneously or a retrograde P wave is present.
• Orthodromic (narrow QRS complex) and antidromic (wide QRS complex) are discussed later.

Cause: It may be:

• A reentry excitation phenomenon as there is anterograde conduction over the slower AV nodal pathway and retrograde conduction over a faster accessory pathway.
• Enhanced automaticity.
• Triggered dysrhythmias.

Clinical Picture: During the episode, patients suffer from lightheadedness, dizziness, fatigue, chest discomfort, dyspnea, and syncope (in 50% of patients). Polyurea usually occurs due to an increase in secretion of atrial natriuretic peptide in response to increased atrial pressure from contraction of the atria against closed AV valves during the dysrhythmia episode. It is 3 times more in women than men.

Treatment:

1. Treatment of the cause.
2. It may resolve spontaneously.
3. Increase the vagal tone by one of the following methods:
   • Carotid sinus massage (unilateral on the right side, usually for 10-20 sec).
   • Eye ball compression.
   • Valsalva maneuver (forced exhalation against a closed glottis i.e., straining) in an awake patient.
   • Facial immersion in cold water.
   • Application of a bag with ice/ice water to the face is the most effective in infants and children.

If vagal stimulation is unsuccessful, give:

4. Adenosine 6-12 mg given as fast i.v. injection over 1-2 seconds is of choice. It has a very rapid onset (15-30 sec) and short duration of (1-2 minutes). It blocks A-V conduction without compromising ventricular function; therefore, it is safe and effective during hemodynamic instability. It is avoided in patients with asthma or AV conduction block.

5. If adenosine is unavailable, the treatment is according to the hemodynamics and presence of ischemia:

Normotensive Patients	Hypotensive or Ischemic Patients
1. Ca^{++} channel blockers such as verapamil or diltiazem. **2. Esmolol:** **3. Other drugs :** • Digitalis • Quinidine • Edrophonium • Procainamide • Propranolol • Phenylephrine (it produces vasoconstriction which in turn increases blood pressure causing a reflex increase in vagal tone).	**Synchronized DC cardioversion** • Synchronized DC is done to avoid occurrence of a DC shock in the vulnerable period of ventricular repolarization (i.e., synchronization allows delivery of the shock simultaneously with an R wave apex.), otherwise ventricular fibrillation may occur. • 25-50 Joules are usually needed. • It Requires light general anesthesia.

6. **Special situations:**

- **PSVT due to digitalis toxicity**:
  - Avoid DC cardioversion as it may cause ventricular arrhythmias.
  - It is treated by phenytoin 100 mg i.v. over 5 min with correction of hypokalemia.
- **Sepsis related or refractory PSVT:**
  - Volume loading.
  - Amiodarone 300 mg i.v. infusion over 20 min.
    then 900 mg i.v. infusion over 24 hours.
- **Thyrotoxicosis :**
  - β blockers.
- **Pheochromocytoma:**
  - α blockers should be given first.
  - β blockers.
- **Recurrent AV nodal reentrant tachycardia especially in Wolf-Parkinson-White syndrome:**
  - **Radiofrequency catheter ablation** is performed where an intracardiac electrode catheter is inserted percutaneously under local anesthesia and conscious sedation into a large vein (e.g., femoral, subclavian, or internal jugular) to produce small, well-demarcated areas of thermal injury that destroy the myocardial tissue responsible for initiation or maintenance of dysrhythmias.

  PSVT is classified into **orthodromic (narrow QRS complex) and antidromic (wide QRS complex)** which are discussed later.

7- Wandering Atrial Pacemaker (Multifocal Atrial Tachycardia):

ECG: • P wave is of different configuration with irregular rhythm (but slower than atrial fibrillation) and there are no F waves.
• PR intervals vary with each QRS complex (i.e., there is irregular ventricular rate).

Cause: Presence of **multiple ectopic pacemakers** in the atrium due to:
• respiratory failure • methylxanthine toxicity (theophylline and caffeine)
• congestive heart failure • sepsis
and • metabolic and electrolyte disturbances.

Treatment:
1- Treatment of the cause e.g., discontinue theophylline.
2- Mg sulfate 2 gm i.v. over 1 hour followed by 1-2 gm i.v. infusion/hour.
3- Verapamil
4- β-blockers such as esmolol
Cardioversion and digoxin are not effective.

8- Atrial Flutter:

ECG: • Heart rate: - Rapid atrial rate 300 beat/min.
- The ventricular rate is irregular and according to the degree of AV conduction
either 1 : 1 flutter i.e. 300/min,
2 : 1 flutter i.e. 150/min (most of patients),
3 : 1 flutter i.e. 100/min,
or 4 : 1 flutter i.e. 75/min.

• P wave: is absent and replaced by the characteristic flutter waves **(F waves)** producing a **Sawtooth pattern.** The flutter waves are not separated by an isoelectric baseline.

Causes: are the same as atrial fibrillation. Atrial flutter may change to atrial fibrillation or conversely atrial fibrillation may convert to atrial flutter. Some authors consider atrial flutter as a more organized form of atrial fibrillation.

Treatment:

a- If the patient is hemodynamically unstable:

- **Synchronized cardioversion** is used usually with less than 50 joules.
- If atrial flutter lasts longer than 2-3 days, the patients should be **anticoagulated** and evaluated by **transesophageal echocardiography** for the presence of atrial thrombus prior to any attempt at cardioversion.

b- If the patient is hemodynamically stable:

- Transesophageal or transvenous right atrial electrode **pacemaker** is used to overdrive the rate and convert the rhythm to sinus rhythm.
- Pharmacological control to control ventricular rate, but none of these drugs converts atrial flutter to sinus rhythm: - i.v. amiodarone.
  - i.v. diltiazem or verapamil.
  - i.v. procainamide especially in severe cases as 1 : 1 AV conduction.

9- Atrial Fibrillation (AF):

ECG:

- Heart rate: - Rapid atrial rate 350-500 beat/min.
  - The ventricular rate is extremely irregular but > 140 /min with healthy A-V junction. It may reach 300 beat/min in patients with accessory bypass tract.
- P wave is absent and replaced by irregularities.
- It may be paroxysmal or chronic sustained rhythm.

Clinical Picture and Complications:

1- It may be asymptomatic.

2- In acute AF, low cardiac output clinical picture may be present such as palpitation, angina, congestive heart failure, pulmonary edema, and hypotension because atrial contraction is responsible for 25% of the ventricular end diastolic volume (preload).

3- In chronic AF, atrial mural thrombosis, usually in the left atrial appendage, may be present and may cause systemic embolization such as stroke (present in 15% of patients with AF for longer than 3 days).

Cause: There are multiple areas of the atria that continuously depolarize and contract in a disorganized manner. Predisposing factors and causes include:

- Valvular heart disease.
- Chronic myocardial ischemia or acute myocardial infarction.
- Cardiomyopathy or pericarditis.
- Chronic obstructive pulmonary disease.
- Acute alcohol intoxication.
- Hypertensive heart disease.
- After cardiac surgery.
- Thyrotoxicosis.
- Pulmonary emboli.
- Atrial septal defect.
- **Idiopathic AF (lone AF)**: is common in relatively young patients (< 60 years) and has no predisposing factor. It is the most common sustained dysrhythmia that occurs in 10% of patients with AF.
- **Paroxysmal AF**: is usually due to **emotional** stress, **vomiting**, or **acute myocardial infarction.**

Treatment:

1- Treatment of the Causes and Predisposing Factors.

2- Cardioversion to Sinus Rhythm:

a- If the patient is **hemodynamically unstable** (hypotensive or ischemic) or there is **a new onset of acute AF** in a previously normal rhythm patient, **synchronized electrical cardioversion** is used:

- It is the most effective method for converting AF to normal sinus rhythm with a success rate of 90%.
- Energy required:
  - For monophasic defibrillators, begin with 100-200 joule (or 50 joule in case of atrial flutter). If additional shocks are needed, increase the energy level of each successive shock by 100 joule until a maximum shock strength of 400 joule is reached. Wait at least one minute between shocks to minimize the risk of cardiac ischemia.
  - For newer biphasic defibrillators, use only half the energy recommended for monophasic shocks.
- It is painful and thus usually done with heavy sedation such as benzodiazepines (e.g., midazolam) and/or an opioid (e.g., morphine or fentanyl).
- Anticoagulation therapy may be given before electric cardioversion (see below).

b- If the patient is **hemodynamically stable** (i.e., no hypotension or ischemia), **pharmacological cardioversion therapy.**

- It is the most effective if initiated within 7 days of the onset of AF.
- For example: amiodarone (especially indicated in patients with significant heart diseases such as ischemic heart, left ventricular hypertrophy or failure), propafenone, ibutilide (some consider it the best agent to convert AF to sinus rhythm) or sotalol.

Nowadays, it is rarely to convert AF to sinus rhythm by using class Ia antiarrhythmic drugs such as quinidine or procainamide, but if they have been used, controlling the ventricular rate must be done by digoxin before their administration as these drugs may accelerate the ventricular rate. Quinidine may nearly result in doubling of the serum digoxin and so may increase digoxin toxicity; therefore, care should be taken. Procainamide does not affect digoxin level; thus it has been better used.

3- Drug Control of the Ventricular Rate:

These drugs produce slow AV nodal conduction, aiming to control ventricular rate to be 80-100 beats/min. They include:

- β-blockers especially esmolol or metoprolol.
- Ca^{++} channel blockers as diltiazem or verapamil.
- Amiodarone can be used also to control ventricular rate.
- Digoxin (0.125-0.25 mg/6 hour i.v.), but it is not effective for conversion of AF to sinus rhythm and not useful in acute rapid AF as its peak of action is delayed for several hours.

4- Anticoagulation Therapy:

Indications:

- Chronic AF.
- For AF lasting > 2-3 days, it is either:
  - The patients should be anticoagulated for 3-4 weeks before electrical cardioversion is attempted.

  or - The patients should be anticoagulated and evaluated by transesophageal echocardiography for presence of atrial thrombus before cardioversion is attempted and then the anticoagulant should continue for 3-4 weeks later after cardioversion (because cardioversion itself may also induce thrombus formation). This regimen avoids waiting 3-4 weeks without cardioversion. This approach is also suitable if the onset of AF is unknown.

The anticoagulant therapy is chosen according to the patient condition:

- Warfarin (to keep INR 2-3): - Age > 75 years or ≥ 60 years with diabetes or coronary artery disease.
  - Heart failure with left ventricular ejection fraction < 0.35, with hypertension, or with thyrotoxicosis.
  - Prosthetic heart valve (mechanical or tissue).
  - Rheumatic mitral valve diseases.
  - Prior history of thromboembolism or strokes.
- Aspirin 325 mg daily: - Age < 60 years with heart disease, but no risk factors (i.e., no heart failure with ejection fraction < 0.35 or with hypertension).
  - Age ≥ 60 years with no risk factors.
  - Contraindications to warfarin.

No anticoagulant therapy is required for patients < 60 years with no heart diseases or risk factors (i.e., lone AF), but some authors still recommend aspirin for these patients.

The mechanism of action, doses, side effects of the previously mentioned drugs are discussed in chapter "Pharmacological Adjuncts during Anesthesia and Intensive Care".

B) Ventricular Dysrhythmias

1- Premature Ventricular Contractions (PVCs) (Ventricular Ectopy or Extra-systole):

ECG:
- **Premature** i.e., it occurs earlier than expected.
- **QRS complex** is wide, aberrant and bizarre in shape and it is ≥ 3 mm in width. It characterized by:
  - **Frequency** (number/min).
  - It may be bigeminy or trigeminy.
  - A **coupling interval** is between the premature ventricular contraction and the preceding normal beat. It is usually fixed, but may be variable.
  - **A compensatory pause** is between the premature ventricular contraction and the next normal beat. It is a fully compensatory pause i.e., interval between the normal QRS complex immediately before and immediately after the premature ventricular contraction is exactly twice the basic RR interval.
  - **PVCs forms**: are either uniform PVCs which are due to a unifocus which may occur in a

healthy individual or in an organic heart lesion, or multiform PVCs which are due to either multifoci or a unifocus, but it indicates an organic heart lesion.

- **R on T phenomenon (premature ventricular contraction on T)**: It occurs when the PVCs occur at or near the T wave peak of the preceding normal beat i.e., in the vulnerable period. It may precipitate ventricular tachycardia or fibrillation. The vulnerable period is the relative refractory period of the cardiac action potential. It occurs at approximately the middle third of the T wave.

Clinical Pictures: palpitation, near syncope, or syncope.

Causes: PVCs occurs due to ectopic foci located below the AV node.

1- Idiopathic: It can occur in normal persons at **rest** and disappear with exercise.

2- Physiological:
- Excessive coffee, tea, or alcohol consumption.
- Increased sympathetic activity.

3- Pathological:
- Cardiovascular diseases as - myocardial ischemia or infarction,
  - myocarditis,
  - hypertension,
  - mitral valve prolapse,
  - or - mechanical irritation of the ventricle e.g., by central venous or pulmonary artery catheter.
- Hypoxemia, hypercarbia, and acidosis.
- Hypokalemia and hypomagnesemia.

4. Pharmacological: • Digitalis toxicity. • Cocaine toxicity.

Treatment:

It is only treated if there is one of the following conditions:

- Frequent > 5/min.
- Bigeminy or trigeminy PVCs.
- Multi-focal PVCs.
- Runs of > 3 consecutive PVCs.
- R on T phenomenon.

As these characteristics are associated with increased risk of ventricular tachycardia or fibrillation; therefore, they should be treated as follows:

1- Treatment of the cause.

2- β-blockers are the most effective.

3- Lignocaine: initial i.v. bolus 1-2 mg/kg followed by 1-4 mg/min (20-50 μg/kg/min) i.v. infusion.

4- Amiodarone, procainamide, and the other antiarrhythmic drugs are indicated only if the PVCs progress to ventricular tachycardia or are associated with hemodynamic instability.

N.B.: If PVCs are associated with a slow atrial rate (escape beat), increase the heart rate by anticholinergic drugs which will lead to disappearance of PVCs.

2- Ventricular Tachycardia (VT): is either:

a) Monomorphic Ventricular Tachycardia:

ECG:
- A run of 3 or more consecutive PVCs.
- Heart rate: 120-250/min with abrupt onset.
- It is either regular or irregular.
- It is either sustained (i.e., > 30 seconds) or paroxysmal.
- QRS complexes are broad. If the heart rate is very rapid, **Sine wave appearance** is present which is called **ventricular flutter**. It usually progresses to ventricular fibrillation.
- P wave is dissociated from the QRS complex i.e., independent atrial activity.

N.B.:

- **Accelerated Idio-Ventricular Rhythm:**

The heart rate is usually between 50-100 beat/min with wide QRS complexes, but without P waves.

- Sometimes it is very difficult to differentiate between supraventricular tachycardia (associated with aberrant or prolonged AV conduction such as right or left bundle branch block) and ventricular tachycardia. They can only be differentiated by:
  - In VT, there is AV dissociation, where there is no fixed relationship between P waves and QRS complexes.
  - In VT, there is fusion beats prior to the onset of the arrhythmias. A fusion beat is an irregularity shaped QRS complex that is caused by retrograde transmission of a ventricular ectopic impulse that merges (fuses) with a normal QRS complex.

Types and Clinical Pictures:

a. VT with pulse: There is usually no hemodynamic instability.

b. Pulseless VT: It is more common. It is a grave dysrhythmia always associated with **hemodynamic instability.** Besides the clinical picture of the cause, there are:

Cannon waves in the jugular venous pulse.
Variable 1st heart sound.
Palpitations and syncope.

Causes:
- Hypovolemia.
- Hypoxia.
- Hydrogen ion (acidosis).
- Hyper-/hypokalemia, other metabolic.
- Hypothermia.
- Heart diseases (infarction, cardiomyopathy, myocarditis, ischemia with a ventricular aneurysm)
- Tablets (drug over dose, accident).
- Tamponade, cardiac.
- Tension pneumothorax.
- Thrombosis, coronary artery disease.
- Thrombosis, pulmonary embolism.

Treatment:

a- VT with Pulse: i.e., with stable hemodynamics.

1- Cardioversion.

2- If persistent after cardioversion, **amiodarone** 150 mg over 10 minutes can be repeated as needed to a maximum total dose of 2.2 gm in 24 hours or infusion 1 mg/min for 6 hours and then 0.5 mg/min for 18 hours.

3- Procainamide, sotalol, bretylium (not available nowadays) and lidocaine can be used.

b- Pulseless VT: It is true emergency condition treated according to the algorithm of cardiopulmonary resuscitation (discussed in the chapter of "Cardio-Pulmonary Resuscitation").

b) Polymorphic Ventricular Tachycardia (Torsade de Pointes)

It is a special form of VT initiated by a premature ventricular contraction in the setting of abnormal ventricular repolarization (i.e., prolongation of the QT interval).

ECG:
- The QRS complex vector (or axis) rotates cyclically i.e., positive for several beats then negative for others then the reverse occurs (Torsade de Pointes means turning or reversal of points).
- Prolonged QT interval. If QT interval is not prolonged, it is not called Torsade de pointes, but it is simply known as polymorphic VT.

Causes: Conditions which prolong ventricular repolarization (i.e., prolonged QT interval or prominent U waves).

1- Pathological:
- Electrolyte disturbances as decreased s. K^+, s. Ca^{++}, s. Mg^{++}.
- Complete heart block.
- Myocardial ischemia.
- Acute myocarditis.
- Liquid protein diet.
- Hypothermia.
- Right radical neck dissection.
- Subarachnoid hemorrhage.

2- Pharmacological: drugs block K^+ channel. All drugs that prolong QT interval.
- Antiarrhythmics: quinidine, procainamide, disopyramide, flecainide, propafenone, sotalol, ibutilide, and amiodarone.
- Antiemetics: cisapride and dolasetron.
- Antipsychotics: haloperidol, thioridazine, droperidol, and chlorpromazine (a phenothiazine).
- Antihistaminics: terfenadine and astemizole.
- Antifungals: ketoconazole and fluconazole.
- Antibiotics: trimethoprim-sulfamethoxazole, clarithromycin, levofloxacin, and erythromycin.
- Antidepressants: amitriptyline, imipramine, and doxepine.
- Anesthetics: volatile agents such as isoflurane and enflurane.

Treatment:

1- Treatment of the cause and stopping possible causing drugs.

I.v. Mg sulfate can decrease or prevent ventricular arrhythmias even in the absence of hypomagnesemia.

2- Cardioversion.

3- Isoproterenol suppresses ectopic beats and shortens QT interval, but it is contraindicated in ischemic heart diseases and congenital prolonged QT syndromes.

4- Temporary cardiac overdrive pacing or automatic implantable cardioverter defibrillator (AICD).

5- β blockers may be useful.

3- Ventricular Fibrillation (VF):

ECG: • QRS complexes are not visible.
• Irregular fibrillation pattern which is either coarse or fine.

Clinical Picture: It is the most common cause of sudden cardiac death. There is no cardiac output resulting in **circulatory collapse.** A pulse or blood pressure never accompanies ventricular fibrillation.

Cause: Due to chaotic asynchronous ventricular contractions which result from the same causes as mentioned above in VT.

Treatment:

• It is a true emergency condition which needs cardiopulmonary resuscitation. The algorithm is discussed in chapter "Cardio-Pulmonary resuscitation".

• Some patients are treated by a permanent insertion of automatic implantable cardioverter defibrillator (AICD).

Perioperative Cardiac Dysrhythmias

I. Preoperative Dysrhythmias:

If dysrhythmia is present, it should be treated preoperatively and postpone surgery if necessary. The types, clinical pictures, ECG pictures, and management of dysrhythmias are discussed above.

II. Intraoperative Dysrhythmias:

Incidence: 12% in patients undergoing anesthesia.
30% in patients with cardiovascular diseases.

Factors Affecting Intraoperative Dysrhythmias:

1. Ventilation Abnormalities:

- **Hypoxemia**: initially, it causes tachycardia.
  Later on, it causes bradycardia.
- **Hypercarbia** produces ventricular extra-systoles.

2. Catecholamines: They cause ventricular dysrhythmias.

- **Endogenous:**
  Inadequate analgesia.
  Inadequate depth of anesthesia.
  Airway manipulation (laryngoscopy, tracheal intubation, and suctioning).
  Hypoxia and hypercarbia.
  Hyperthyroidism.
  Pheochromocytoma.
- **Exogenous:**
  Sympathomimetics as adrenaline or ephedrine.
  Adrenaline containing local anesthetics especially with halothane and hypercarbia.

3. Electrolyte Disturbances:

- **Hypokalemia** causes ventricular dysrhythmias because it increases ventricular irritability especially in:
  Ischemic heart diseases.
  Patients receiving digoxin.
  Hyperventilation which causes hypocapnia. This results in respiratory alkalosis which causes K^+ shift into cells producing more hypokalemia (serum K^+ decreases by 0.5 mmol/L for every 1.3 KPa "10 mm Hg" decrease in CO_2 tension).
- **Hyperkalemia** causes an AV conduction block up to cardiac arrest especially with:
  Patients with renal impairment.
  The usage of suxamethonium in patients with burns, denervating injuries, paraplegia, or myopathies as it shifts K^+ out from muscle cells.

4. Malignant Hyperthermia:

The most consistent early sign is unexplained and progressive tachycardia. Ventricular dysrhythmias occur later.

5. Surgical Causes: especially with light anesthesia.

- Eye surgery (oculo-cardiac reflex) especially squint surgery.
- Anal stretch.
- Mesenteric traction.

These three causes increase vagal tone producing bradyarrhythmias due to parasympathetic stimulation.

- Pharyngeal or laryngeal surgery.
- Dental surgery (partially blocked by local anesthesia infiltrations).

Both cause tachyarrhythmias due to sympathetic stimulation.

- Direct cardiac stimulation: such as chest surgery or right heart catheterization with a pulmonary artery catheter usually causes PVCs.

N.B.: Reflex Dysrhythmias:

It occurs during light anesthesia due to sympathetic or parasympathetic stimulation. It includes **all the surgical causes except direct cardiac stimulation**. It is prevented by deepening the anesthesia.

Reflex tachycardia (during hypotension) and **reflex bradycardia "Cushing reflex"** (during increased intracranial tension) are also considered reflex dysrhythmias.

6. Cardiac Diseases:

- Already existing dysrhythmias.
- Congestive heart failure.
- Ischemic heart diseases.
- Valvular heart disease.
- Myocarditis.
- Cardiomyopathy.

7. Drugs:

- Anesthetic drugs: (especially with hypercarbia) as halothane and enflurane may produce junctional rhythm.
- Ketamine blocks the reuptake of catecholamines producing tachyarrhythmias.
- Muscle relaxants: - Suxamethonium causes bradycardia on repeated doses due to vagal stimulation.
  - Nondepolarizing muscle relaxants as pancuronium cause a vagolytic effect.
- Sympathomimetic drugs: as adrenaline and ephedrine.
- Methyl-xanthines: as aminophylline.
- Tricyclic antidepressants.
- Phenothiazines.
- Monoamino oxidase inhibitors (MAOIs).
- Digoxin: especially in hypokalemic patients or those with renal impairment.

Management:

- Continuous intraoperative ECG monitoring is mandatory especially lead II.
- Hemodynamic status should be assessed.
- Correct the predisposing factors at first. It may be the only treatment.
- Active treatment such as antiarrhythmics and cardioversion are generally indicated if:
  - The dysrhythmias predispose to ventricular tachycardia or VF.
  - The dysrhythmias cause significant hemodynamic effects.
  - The dysrhythmias are associated with myocardial ischemia.

The types and treatments of dysrhythmias are discussed above.

III. Postoperative Dysrhythmias:

Causes:

- Residual anesthetic agents especially halothane.
- Hypoxemia.
- Hypercarbia.
- Electrolyte or acid-base disturbances.
- Myocardial ischemia or infarction.
- Postoperative pain.
- Full bladder.
- Vagal stimulation e.g., by an endotracheal tube or a suction catheter.

Ventricular Preexcitation Syndromes

Incidence: 0.1- 0.3% of general population.

Pathophysiology:

It is characterized by premature activation of a portion of the ventricles by cardiac impulses that travel from the atria to the ventricles via an accessory (anomalous) conduction pathway (bypass tracts) (figure 13-35).

Three accessory conduction pathways are identified:

Name	Accessory Pathway	ECG Findings
Kent fibers (Wolf-Parkinson-White syndrome) (WPW) (The most common)	**Atrio-ventricular** bundle (i.e., from the atrium to the ventricle)	• Short PR interval < 0.12 sec. • Wide QRS complex > 0.12 sec. • Delta wave.
James fibers (Lown-Ganong-Levine syndrome)	**Intra-nodal** bypass tract (i.e., it bypasses the AV node and is inserted directly into the bundle of His causing loss of the normal physiological delay of the AV node).	• Short PR interval < 0.12 sec. • Normal QRS complex. • No delta wave. + Atrial flutter or AF.
Mahain fibers	Either: **Nodo-ventricular** bundle (i.e., from AV node to the ventricle) or **fasciculo-ventricular** bundle (i.e., from His bundle or a bundle branch to the ventricle).	• Normal or slight short PR interval. • Wide QRS complex. • Delta wave. (it is misdiagnosed as bundle branch block).

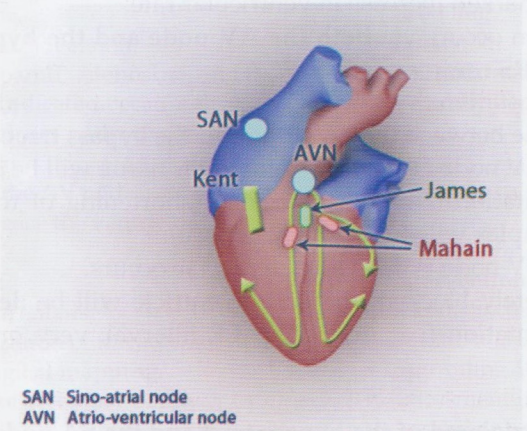


Figure 13-35: Accessory conduction bypass-tracts

The pathway of the Impulses from the Atrium to the Ventricle can be as Follows:

1- **In the Normal Sinus Rhythm**, the cardiac impulses are partly conducted via the AV node and partly via the more rapidly conducting accessory conduction pathway causing **early ventricular depolarization** which causes: • Short PR interval.

- **Delta wave (slurred initial deflection in the QRS complex)**.
- Slightly wide QRS complexes due to fusion of the complexes of the normal and abnormal ventricular depolarization.
- ST segment and T wave changes due to abnormal ventricular repolarization.

N.B.: The accessory bundle differs from the AV node in:

- Conduction which occurs in both directions. It is either:
  - retrograde i.e., from the ventricles to the atria (more common),
  or - antegrade i.e., from the atria to the ventricles (very rare).
- It lacks the rate-limiting property.
- If an atrial premature beat passes via the bypass tract and reaches the ventricle at its vulnerable period, ventricular fibrillation may occur.

2- During Reentry Dysrhythmias:

Due to the difference in the conduction speeds and relative refractory periods of the AV node and accessory bundle, **a reentry circuit** occurs, causing paroxysms as AV nodal reentrant tachycardia (the most common), atrial flutter and AF in 20-50% of patients.

The impulses form the atrium to the ventricle pass through one of the following pathways:

a- Impulses pass **from the atrium to the ventricle** through the **normal AV nodal-His-Purkinje system** and return back from the ventricle to the atrium through the accessory bypass-tract (i.e., retrograde conduction via the accessory fibers). This is the most common pathway (90-95% of patients). It produces

normal QRS complexes during AF or AV nodal reentrant tachycardia. The latter is sometimes called "**narrow QRS complex or orthodromic reentrant tachycardia**" which is treated as before in treatment of supraventricular reentrant tachycardia by vagal maneuvers, adenosine, verapamil, or β blockers.

b- Impulses pass **from the atrium to the ventricle** through the accessory bypass-tract (i.e., antegrade conduction) and return back from the ventricle to the atrium through the normal AV node. This is the less common pathway. It produces wide bizarre shaped QRS complexes during AF or AV nodal reentrant tachycardia. The latter is sometimes called "**wide QRS complex or antidromic reentrant tachycardia**". The wide QRS complex seen in antidromic AV nodal reentrant tachycardia makes it difficult to distinguish this dysrhythmia from ventricular tachycardia on the ECG. Wide QRS complex or antidromic reentrant tachycardia is treated by **procainamide** i.v. 10 mg/kg infusion at a rate 50 mg/min or less which is effective because it slows conduction along the accessory pathway and may slow the ventricular response rate and terminate the antidromic dysrhythmia. Electrical cardioversion is used if the ventricular response cannot be controlled by drug therapy and in presence of hemodynamic instability.

N.B.: Adenosine, verapamil, β blockers, and digoxin will not be effective in treatment of antidromic type as they slow AV nodal conduction, but may increase conduction along the accessory pathway. As a result, they may produce a marked increase in ventricular rate.

c- Sometimes, the conduction occurs **via both the AV node and the bypass-tract** causing a mixture of normal, fused and bizarre QRS complexes.

Factors Affecting the Degree of Preexcitation:

1. **The relative conduction time** between the AV node and the bypass tract.
   - If the conduction via the AV node is fast, less ventricular tissue will be depolarized by the bypass tract causing less prominent excitation (i.e., less prominent shortening of the PR interval, less prominent delta wave and the QRS complex will be relatively normal).
   - If the conduction via the AV node is delayed, the reverse occurs.
   - If the AV node is completely blocked, the entire ventricle will be depolarized by the bypass tract, causing very prominent excitation (i.e., very short PR interval, very prominent delta wave and very bizarre wide QRS complexes).
2. **Inter-atrial conduction time**.
3. **The distance between the atrial end of the bypass tract and the SA node.**
4. **The autonomic tone**: as increased heart rate causes more delayed AV node conduction producing more prominent pre-excitation.

Prolonged QT Interval Syndrome

Causes and Pathophysiology:

1- Congenital: • with deafness (Jervell and Lang Nielson syndrome): autosomal recessive.
• without deafness (Romano-Ward syndrome): autosomal dominant.

Due to an imbalance in the sympathetic innervation of the heart (increased left cardiac sympathetic activity or decreased right cardiac sympathetic activity).

2- Acquired: the same causes as Torsade de pointes (see above).

There are 3 types: • Type I and II are one of the K^+ channelopathies.
• Type III is one of the Na^+ channelopathies.

The following table compares the most important pre-excitation syndromes, the "WPW syndrome" and the prolonged QT interval syndrome.

	Wolf-Parkinson White (WPW) Syndrome	Prolonged QT Interval Syndrome
ECG	• Short PR interval (< 0.12 sec). • Wide QRS complex (> 0.12 sec). • Delta wave.	• Prolonged rate-corrected QT (QTc) interval > 0.44 sec even when corrected for heart rate (because the QT length changes with heart rate change). • Polymorphic ventricular tachycardia (Torsade de pointes). N.B.: QTc is obtained by dividing the QT interval by the square root of the RR interval i.e., $= \frac{QT}{\sqrt{\ }}$ =< 0.44 sec normally.

Clinical picture	• Patients are **young** and usually have good myocardial function. • In rare cases, **syncope, congestive heart failure** or both may occur with rapid heart rate. • In 20-50% of patients, **PSVT** (palpitations with or without syncope), **atrial flutter, and AF** may occur. • In 12% of patients, **sudden death** may occur (due to ventricular tachycardia). • **Associated anomalies** as Ebstein's anomaly, mitral valve prolapse, or cardiomyopathy may occur.	• Patients are either **young or elderly.** • **Syncope:** may occur in the early childhood (congenital type) and may be confused with seizures. It is triggered and increased by sympathetic stimulation as exercise, stress, emotions, or fright. • **Sudden death** may occur (occasionally due to ventricular tachycardia).
Treatment	1- **Medical therapy:** Aim: **is to decrease cardiac sympathetic activity** which decreases the conduction rate and increases the relative refractory period (RRP) of the bypass tract. a- **PSVT**: treated as above. b- **AF**: • Procainamide. • Amiodarone. • Electrical cardioversion. **N.B.: Digoxin, verapamil, adenosine, and β-blockers are contraindicated** because they decrease: • RRP of the accessory pathway (increase its conduction). • Conduction in the AV node. Therefore, both increase the ventricular response causing VT and VF. 2- **Surgical therapy:** Operative procedure entails: • Anatomical localization of the accessory pathway by **electro-physiological mapping.** • **Interruption of the accessory pathway** by **- Cryoablation.** **- Laser coagulation.** **- Endocardial resection.** **- Encircling ventriculotomy**. Electro-physiological mapping is done before cardiopulmonary bypass (CPB) or with the support of normothermic CPB. If ventricular tachy-arrhythmia is induced, surgical ablation is done under CPB.	1- **Medical therapy:** Aim: **is to decrease cardiac sympathetic activity.** a- β blockers (except sotalol as it has intrinsic sympathetic activity): They shorten the QT interval and decrease the sympathetic activity, but they increase the threshold of VF. b- Verapamil. Bretylium. Phenytoin. **N.B.: Procainamide and quinidine are contraindicated** as they prolong the QT interval. 2- **Interventional therapy: Left stellate ganglion block:** It shortens QT interval transiently; therefore, it is used in: • Controlling acute cardiac arrhythmias. • Assessment if surgical ganglionectomy will be successful or not. • Preoperative patient preparation. **Pacemaker insertion** is indicated **in congenital** long QT syndrome.
Anesthetic management	**Aim**: **Avoiding sympathetic stimulation** So; • avoid light anesthesia, hypercarbia, acidosis, transient hypoxia, pain, or anxiety. • avoid hypovolemia. • avoid digitalis or verapamil. • avoid anticholinergics or sympathomimetics.	**Aim**: **Avoiding sympathetic stimulation** So: • avoid light anesthesia, hypercarbia, acidosis, transient hypoxia, pain, or anxiety. • avoid hypovolemia. • avoid causes that increase QT interval as above. • avoid acute hypokalemia (due to hyperventilation).
Pre-operative	• Preoperative assessment: as above. • Premedications: Anxiolytics e.g., benzodiazepines. Prophylactic β blockers as esmolol. Avoid anticholinergics.	• Preoperative assessment as above. • Premedications: as WPW syndrome. **Prophylactic left stellate ganglion block** can be done.
Intra-operative	The same anesthetic principals are applied for both WPW syndrome and prolonged QT interval syndrome. **Monitoring:** Besides the standard monitors, • Invasive blood pressure monitoring. • Central venous and pulmonary artery catheterization (they may predispose to PSVT). **Intubation:** should be in a deeply anesthetized patient and the pressor response to intubation should be decreased by measures such as fentanyl…etc.	

	Induction: • Barbiturates can be used. • Ketamine is avoided. **Maintenance:** • N_2O can be used. • Opioids can be used. • Volatiles can be used because: They decrease sympathetic stimulation and increase the RRP in both the AV node and the accessory pathway (enflurane > isoflurane > halothane). Isoflurane and halothane increase the coupling interval (which is a measure of the liability of a premature beat to induce tachycardia); therefore, enflurane is of choice, but it is rarely used nowadays. • Muscle relaxants: - Atracurium, cis-atracurium, and vecuronium are of choice. - Avoid pancuronium as it increases sympathetic stimulation. • The reverse of muscle relaxant is better avoided. • Electric cardioversion and antiarrhythmic drugs should be available. **Extubation:** should be deep. Phenytoin is given orally in the postoperative period in prolonged QT interval syndrome because it shortens QT interval.

N.B.: Causes of Short PR Interval:

- Preexcitation syndrome: The P wave is normal during sinus rhythm.
- Lower atrial or upper AV junctional rhythm: A retrograde P wave is present.

N.B.: Causes of short QT interval:

- Electrolyte disturbances e.g., increased s.Ca^{++}
- Digitalis.

Heart Block

Causes

1. Organic Diseases:

1- Diseases affecting the **conductive tissues** especially:
- Lenègre's disease: **sclero-degenerative changes** of the terminal portions of the bundle of His.
- Lev's disease: **fibrous encroachment** of the proximal portion of the bundle of His.

2- Diseases affecting the **cardiac tissue:**
- Myocardial ischemia or acute infarction (especially in the distribution of the right coronary artery).
- Myocarditis.
- Cardiomyopathies especially with restrictive physiology such as sarcoidosis, mononucleosis, and amyloidosis.
- Ventricular hypertrophy due to: - Valvular heart diseases.
  - Aortic stenosis, aortic regurgitation causing right or left bundle branch block.
  - Pulmonary hypertension causing right bundle branch block.
  - Systemic hypertension causing left bundle branch block.

3- Surgically produced **(iatrogenic).**

4- **Congenital** heart diseases.

2. Functional Disturbances:

1- Increased **vagal tone.**

2- **Drugs:** • Digitalis toxicity. • Quinidine. • Procainamide.
• β-blockers. • Ca^{++} channel blocker toxicity.

3- **Hyperkalemia.**

4- It may occur in **normal patients**, but rarely.

Classification

1. 1st Degree Heart Block:

Cause: due to conduction block in the AV node itself.

Clinical Picture: The condition is asymptomatic and only diagnosed by ECG.

ECG: prolonged PR interval > 0.2 seconds.
Treatment: No treatment is needed before anesthesia.

2. 2nd Degree Heart Block:

Some atrial impulses fail to reach the ventricle producing dropped beats.

a) Mobitz Type I (Wenckebach's Phenomena):

Cause: due to gradual fatigue of the AV bundle with recovery following a rest period when the dropped beat occurs.
Clinical Picture: The condition is asymptomatic and only diagnosed by ECG.
ECG: gradual progressive prolongation of the successive PR intervals followed by a dropped beat i.e., a P wave is not followed by a QRS complex.
Treatment: Atropine, isoprenaline, or dopamine. If they are unsuccessful, temporary pacemaker may be indicated. Increased mortality is now recognized if not paced.

b) Mobitz Type II:

Cause: due to a complete interruption in the conduction a cardiac impulse, usually at a point below the AV node in the bundle of His or in a bundle branch (i.e., in the infra-nodal conduction system).
Clinical Picture: asymptomatic or there are palpitations and near syncope may be present. It is more serious than Mobitz type I because it frequently progresses to complete AV heart block.
ECG:
- PR interval is constant.
- Some of the P waves are not conducted i.e., the numbers of P waves are > QRS complexes.
- When atrial and ventricular contractions are in a ratio of 2:1 or 3:1, the pulse is slow and regular. When atrial and ventricular contractions are in more complex ratios as 3:2 or 4:3, the pulse is irregular with dropped beats.

Treatment:
Preoperative insertion of an artificial, temporary and may be permanent, cardiac pacemaker is justified even in the absence of symptoms. Atropine is usually ineffective.

3. Left Bundle Branch Block (LBBB): It is either complete or incomplete.

a) Complete LBBB:

Cause: due to failure of conduction via the left bundle branch (as above).
ECG:
- QRS width is ≥ 4 mm (i.e., complete) (normal QRS width is ≤ 2.5 mm).
- V_1 shows wide (± notched) negative QS (± small r).
- V_6 shows wide (± notched) positive R (no small q).
- T wave inversion in left chest leads (a secondary change) occurs if T wave inversion (a primary change) occurs in right chest leads e.g., ischemia.
- It decreases ECG evidence of myocardial infarction.

N.B.: ECG of the pacemaker pattern gives picture of LBBB with a pacemaker spike before the QRS complex.
Treatment: It usually needs a pacemaker as it has 6% incidence to progress to complete heart block.

b) Incomplete LBBB (Unifascicular Block): It is either left anterior or left posterior block.

1. Left Anterior (Fascicular) Hemiblock:

ECG:
- As above with LBBB except QRS width is 2.5 – 4 mm (i.e., incomplete).
- + • QRS axis is ≥ - 45 i.e., left axis deviation (the S wave in aVF equals or exceeds the R wave in L_I).

Treatment: No treatment if it is isolated.

2. Left Posterior (Fascicular) Hemiblock:

ECG:
- As above with LBBB except QRS width is 2.5 – 4 mm (i.e., incomplete).
- + • QRS axis is ≥ +120 i.e., right axis deviation.

Treatment: No treatment if it is isolated.

4. Right Bundle Branch Block (RBBB):

ECG:
- V_1 shows rSR` complex with a wide R`.
- V_6 shows qRS complex.
- T wave inversion in right chest leads (a secondary change) occurs if T wave inversion (a primary change) occurs in left chest leads e.g., ischemia.

Treatment: No treatment if it is isolated.

5. Bi-Fascicular Block:

It is RBBB with either left anterior or left posterior hemiblock.
ECG: is either: • RBBB with left anterior hemiblock. It appears as RBBB with left axis deviation.

• RBBB with left posterior hemiblock. It appears as RBBB with right axis deviation.

Treatment: Asymptomatic patients very rarely progress to complete heart block before anesthesia; therefore, implantation of a permanent or temporary pacemaker is unnecessary, but an external pacemaker should be available in the operating room.

6. 3rd Degree Heart Block (Complete Heart Block): (Complete AV Block) (Tri-Fascicular Block):

Clinical Picture:

- Venous cannon waves may be present.
- **Adam-Stokes attacks**: They are episodes of ventricular asystole. They are characterized by light headedness, dizziness, rapid loss of consciousness, and convulsions (in contrast to epilepsy, there is rapid recovery once the heart starts to beat again).
- Congestive heart failure may occur if the stroke volume is unable to offset the decreased cardiac output produced by the severe bradycardia of the AV block.

Cause:

All impulses from the atria are not conducted to the ventricles; therefore, there is no relationship between atrial and ventricular contraction. It is either acquired or congenital.

It occurs in 8% of patients with acute inferior wall myocardial infarction where the heart block is usually transient, although it may last for several days.

ECG:

- There is no relation between P waves and QRS complexes, where the atrial rate is regular and faster than the ventricular rate which is also regular.
- The PR interval is completely variable.
- It is either continuous or intermittent.
- It is of 2 types: - Complete AV nodal block: QRS complexes are normal in shape. Heart rate is 45-55 beat/min and regular.
  - Complete infra-nodal block: QRS complexes are wide. Heart rate is 30-40 beat/min, regular and does not vary with exercise.

Treatment:

1- A permanent artificial cardiac pacemaker is mandatory (unless congenital).

2- Before general anesthesia, a temporary pacemaker should be inserted.

3- In an emergency, **a pharmacological pacemaker: isoprenaline i.v. infusion** is used. Its dose should be adjusted according to the response. It may maintain an adequate ventricular rate until a pacemaker is inserted. For the mechanism of action, side effects, and doses see chapter "Pharmacological Adjuncts to Anesthesia & Intensive Care".

Avoid antiarrhythmic drugs in the absence of the pacemaker.

Anesthetic Management of a Patient with Heart Block

Preoperative Management:

1- Determine **the type** of heart block by ECG and **symptoms** such as congestive heart failure or syncopal attacks.

2- **Avoid drugs** that slow AV conduction as β blockers, digoxin, or verapamil and use drugs that fasten AV conduction as isoprenaline or atropine.

3- Indications of **a temporary or permanent pacemaker:** are discussed later.

Intraoperative Management:

- **Monitoring**: besides the standard monitors particularly the ECG, other invasive monitors can be added according to the condition of the patient.
- **A standby pacemaker** should be available.
- Care is taken to **avoid blood loss and/or hypotension** and also or **using vasodilators** because the heart rate cannot increased.

Postoperative Management:

A decision whether a permanent pacemaker is needed or not should be made by a cardiologist after the immediate postoperative period.

Anesthetic Management of a Patient with Pacemaker or a Patient Undergoing Pacemaker Insertion is discussed later.

Defibrillator (Cardioverter), DC Shock (Electric Cardioversion)

Indications

Cardioversion is indicated in either: • elective cases for chronic arrhythmias,
or • emergency cases for life threatening arrhythmias.

They are used to convert the following arrhythmias to sinus rhythm:

- Ventricular tachycardia (VT).
- Ventricular fibrillation (VF).
- Paroxysmal supraventricular tachycardia (PSVT).
- Atrial flutter.
- Atrial fibrillation (AF) especially: - symptomatic AF < 12 months duration.
  - with history of embolism.
  - with recent onset.
  - not responding to medical treatment.

N.B.: **Cardioversion is not effective** for:

- arrhythmias produced from enhanced automaticity **(i.e., multi-focal atrial tachycardia),**

and • triggered activity **(i.e., digitalis induced arrhythmias)**.

Cardioversion can even trigger more serious ventricular arrhythmias.

Anesthetic Management in elective cases:

Pre-anesthetic Management:

Patient Preparation:

1- **Assess and manage preexisting diseases** such as rheumatic heart diseases, atherosclerotic heart diseases, myocardial infarction, congestive heart failure, or cerebro-vascular occlusive diseases.

2- Patients should **fast for 6-8 hours** before the procedure as usual recommendations.

3- Drugs:

- **Digitalis** therapy predisposes to post-cardioversion arrhythmias; therefore, in some centers, it is withheld for at least 24 hours before cardioversion, but in other centers, withholding digitalis is not necessary as long as there is no evidence of toxicity.
- **Anticoagulant therapy** should be given prophylactically for **3-4 weeks before electrical cardioversion** even in the absence of intracardiac thrombosis because electrical cardioversion may induce thrombosis. **Indications of anticoagulants** in patients with atrial fibrillation are discussed above in the treatment of atrial fibrillation.

4- **Preoperative investigations:** besides the routine investigations more investigations are needed according to the patient's condition such as:

- Electrolyte and acid-base abnormalities that should be corrected as they may contribute to the arrhythmias and their recurrence.
- A 12 lead ECG performed:
  - Immediately before the procedure to confirm that the arrhythmia is still present.
  - Immediately after the procedure to detect any new arrhythmia.

5- **Premedications:**

- Sedation is needed to decrease the circulatory endogenous catecholamines concentration.
- Atropine should be avoided.

6- **The place for performance of cardioversion in elective cases:**

Cardioversion should be done only in areas where **a full range of cardiopulmonary resuscitation** including drugs, cardiac pacing capabilities and airway management are available e.g., intensive care units, emergency rooms, or recovery rooms.

Anesthetic Management:

Monitoring:

- The minimum monitoring consists of an ECG, noninvasive blood pressure, and pulse oximetry.
- The level of consciousness should be monitored, best by maintaining continuous verbal contact with the patient.

Choice of Anesthesia:

Heavy sedation or light general anesthesia is usually required.

Preoxygenation with 100% O_2 for 1-2 minutes is advised.

Induction:

• Short acting agents such as propofol, etomidate or benzodiazepines (midazolam or diazepam) in small increments every 2-3 min (if necessary) are used to maintain cardiovascular stability.

• When the patient is insensible detected by loss of verbal contact with the patient or loss of eyelid reflex (used by some anesthesiologists), secure the airway and give O_2 by a suitable breathing system, and apply the shock which usually arouses the patient.

If **repeated shocks** are required, incremental doses of anesthetics may be given where transient airway obstruction or apnea may occur.

Post-Anesthetic Management:

Monitoring of patients should be continued during the immediate postoperative period for

• recurrence of arrhythmias or • occurrence of complications.

Complications of cardioversion:

• Transient myocardial depression.

• Post-shock arrhythmias e.g., VF.

They may occur even with proper synchronization especially if there is one of the following conditions: hypokalemia, ischemia, digitalis toxicity, and QT prolongation.

• Systemic embolization especially in high risk patients because the electric cardioversion causes cardioversion.

The Physical Principles and Technique are discussed in the chapter of "Basic Physics for Anesthesia & Intensive Care".

Cardiac Pacemakers

It is an electronic device which can artificially pace the heart; so, the myocardium will contract when stimulated.

It was invented in the 1950s.

N.B.: **Implanted Electrical Devices (Gadgets):** devices with an impulse generator and leads which are usually implanted in the chest or abdomen. They include:

• Pacemakers.
• Automatic implantable cardioverter defibrillator (AICD).
• Spinal stimulators for chronic pain control.
• Thalamic stimulation to control Parkinson's disease.
• Phrenic nerve stimulation to stimulate the diaphragm in paralyzed patients.
• Vagus nerve stimulation to control epilepsy and sleep.
• Intravenous pumps.
• Bladder stimulators for neurogenic bladder.
• Gastric stimulators for treatment of obesity.

Therefore, not all subcutaneous devices are pacemakers.

N.B.: Cardiac rhythm management devices include:

• pacemaker,
and • automatic implantable cardioverter defibrillator (AICD)

Indications of pacemakers

1) Heart block:

a. 2nd Degree Heart Block:

- Mobitz type I: is often transient and rarely necessitates pacing.
- Mobitz type II:

• It usually indicates destruction of the conduction system at the level of or below the bundle of His and it usually progresses to a complete AV block.

• Temporary pacing is indicated: - before general anesthesia, and - for acute management, with subsequent implantation of a permanent pacemaker.

N.B.: 1st degree heart block does not need a pacemaker.

b. Left Bundle Branch Block (LBBB):

- Complete LBBB: Requirement of a pacemaker is according to the patient's condition.
- Incomplete (uni-fascicular) LBBB: It does not need a pacemaker if it is isolated.

c. Right Bundle Branch Block (RBBB):

- It does not need a pacemaker if it is isolated.

d. **Bi-Fascicular Block:**
- A pacemaker is indicated only if it is symptomatic as it may progress to complete heart block.
- Asymptomatic patients usually do not need a pacemaker, but an external pacemaker should be available in the operating room.

e. **Complete Heart Block (CHB):** with Stokes-Adams attacks are the second most common indication.

f. **Heart Block with Acute Myocardial Infarction:** especially; - anteroseptal infarction,
and - inferior infarction.

2) Bradyarrhythmias:

a. Severe sinus bradycardia:

e.g.: • After myocardial infarction or after open cardiac surgery.
• During instances of profuse vagotonia.
• Hypersensitive carotid sinus syndrome.
• Overdoses of drugs affecting the conduction system, such as cholinergic agents, Ca^{++} channel blockers, β adrenergic blockers, and digoxin.

b. AF with slow ventricular response not responding to drug therapy.

c. **Sick sinus syndrome is the most common indication**. It usually occurs in elderly patients.

3) Tachyarrhythmias:

Hemodynamically disabling tachyarrhythmias with:
• Resistance or intolerance to drug therapy in conditions where cardioversion is relatively contraindicated such as digoxin therapy.
• Resistance to cardioversion e.g., paroxysmal supraventricular tachycardia and VF.

Pacing at a rapid rate may overdrive the tachyarrhythmias.

4) Other Indications:

• **Long QT syndrome** especially **congenital type**.
• **Dual (bi-ventricular) pacing**; sometimes called "**Cardiac Resynchronization Therapy (CRT)**", where the coronary sinus is catheterized and a ventricular lead is introduced to gain access to the left ventricular muscle. It is indicated in - hypertrophic obstructive cardiomyopathy,
and - dilated cardiomyopathy,
which are refractory to medical treatment (i.e., symptoms at rest or with minimal exertion, left ventricular ejection fraction < 35%, left ventricular dilation, prolongation of the QRS complex > 130 msec).
• **Dual (bi-atrial) pacing**; is being investigated to prevent atrial fibrillation.

Choice of Pacing Mode

The choice of pacing mode depends on the primary indication for the artificial pacemaker.

Pathology	Mode of the Pacemaker Selected
• SA node disease and no evidence of disease of the AV node or bundle of His	AAI pacemaker
• SA node diseases with disease of the AV node or bundle of His • The need for drug treatment to slow AV nodal conduction • Neuro-cardiogenic syncope (due to carotid sinus hypersensitivity) • Vasovagal syncope or • Hypertrophic cardiomyopathy	Dual-chamber (DDD or DDI) pacemaker
• SA node disease, AV node disease, or lower conduction system disease whose heart rates do not increase in response to increase in metabolic demands	Programmable (rate-responsive or rate adaptive) pacemaker
• SA node disease or AV node disease with symptomatic bradycardia	VVI pacemaker
• Cardiac resynchronization therapy as in hypertrophic cardiomyopathy or dilated cardiomyopathy which are refractory to medical treatment.	Dual (bi-ventricular) pacemaker
• Atrial fibrillation	Dual (bi-atrial) pacemaker

The code identification of the pacemakers is discussed in the chapter of "Basic Physics for Anesthesia & Intensive care".

Anesthetic Management

Anesthetic management with pacemakers is required either for patients undergoing placement of pacemaker or for patients with pacemakers undergoing non-cardiac procedures.

A) Anesthetic Management of a Patient with a Permanent Pacemaker Undergoing Surgery

Preoperative Management:

Preoperative Patient Evaluation:

1- The **cause and the date of the insertion** of the pacemaker and **the last test date** should be asked for and evaluated. The manufacturer's identification card from the patient is very helpful.

2- The **pacemaker should be evaluated.** This should be done **by a specialist,** at regular intervals, whose **reports** should be checked preoperatively **by the anesthesiologist**. The pacemaker should be evaluated for:

- **Type and mode of action of the pacemaker** (programmable or not).
- **Proper function**.
- **Battery**: A 10% decrease in heart rate from the initial fixed discharge rate may reflect battery failure.
- **Diaphragmatic or skeletal muscle stimulation:** This occurs if the output from the pacemaker is large. Therefore, the pacemaker output should be adjusted and decreased to avoid this problem.
- **The effect of magnet application (Pacemaker magnet behavior):** The response of the pacemaker to the magnet differs according to the pacemaker type. Some types of pacemakers are converted from a synchronous to **an asynchronous (fixed rate) mode** (most of pacemakers), pacing at a rate which may be higher, the same, or lower than the preset rate. Other pacemakers may show **no change** in **rhythm or rate**. Other types of pacemakers may show **failure for pacing**. Therefore, it is **no longer acceptable to use a magnet routinely** over the pacemaker generator, but **calling the manufacturer or revising the pamphlet** of the device is the most reliable method for determining magnet response.

  A magnet should not be used with programmable pacemakers, because this may permit **random reprogramming** by the electrocautery, because the magnet will turn on a receiver that enables programming of the pacemaker; therefore, the random radio signals sent by the electrocautery (especially spark-gap type unipolar electrocautery) will affect the receiver and produce reprogramming.

3- **The availability of a programmer** for this specific pacemaker device.

4- **Pacemaker syndrome:** This is a physiological disorder caused by a ventricular-inhibited pacemaker (VVI) implanted in a patient with intact ventriculo-atrial conduction; so, a retrograde P wave or ventriculo-atrial conduction follows each paced QRS complex. In some patients, this retrograde atrial conduction may decrease the cardiac output and cause **systemic hypoperfusion**; therefore, vertigo, light headedness, syncope and hypotension may occur. Therefore, DVI pacemaker may be used to avoid this problem.

5- **Pain over the pulse generator pocket** may be due to infection or tissue erosion.

6- **History of anticoagulation:** Because patients with congestive heart failure with a cardiac pacemaker may receive anticoagulant therapy, **precautions** must be taken when **regional anesthesia** is intended to be used.

7- Patients should be evaluated for the presence of **coexisting diseases.**

Preoperative Investigations:

Besides the standard preoperative investigations which are chosen according to the patient condition, the following investigations are important as regards the pacemakers.

1- Twelve Lead ECG: can give the following information about the pacemaker:

- **The pacemaker rate** can be identified by counting the number of spikes per a certain period of time.
- **Absence or attenuated pacemaker spikes** may indicate battery failure, electrical short circuit, or lead fracture.
- **Presence of pacemaker spikes not followed by a paced QRS complex or P wave,** suggests failure to capture or to induce pacing.
- **The paced chamber** can be determined by detecting the relation of the **pacemaker spikes** to the spontaneous and paced QRS complexes or P waves (figure 13-36, 13-37, and 13-38).
  - Atrial pacing: An electrical spike appears before the P wave and QRS morphology is usually normal.
  - Ventricular pacing: An electrical spike appears before the QRS complex which is widened.

- AV sequential pacing: There are 2 electrical spikes, one before the P wave and the other before the QRS complex.

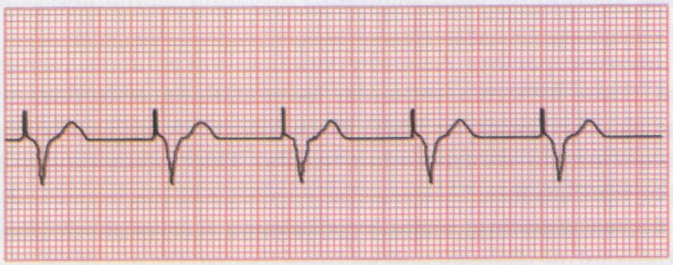


Figure 13-36: ECG of ventricular pacing; pacemaker spikes occur before wide QRS complexes

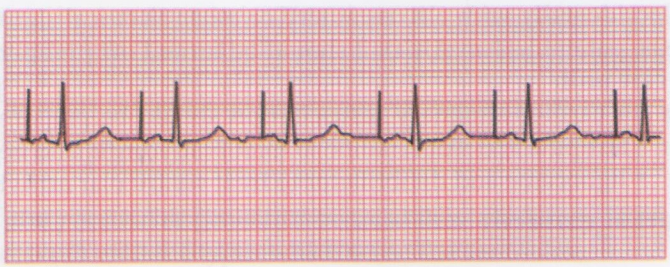


Figure 13-37: ECG of atrial pacing; pacemaker spikes occur before P waves with normal QRS complexes

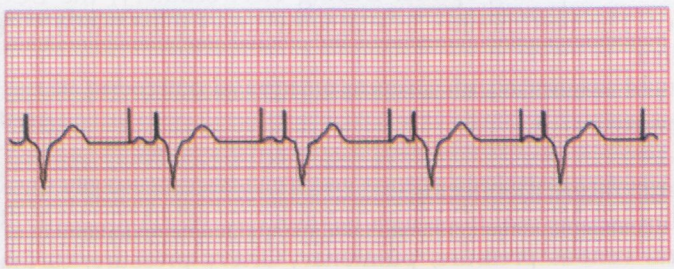


Figure 13-38: ECG of AV sequential pacing

- **The position of the pacemaker leads** can be determined by the QRS morphology:
  If the pacing lead is present in the right ventricle, the paced QRS complex should show left bundle branch block pattern because the electricity reaches the left ventricle from the abnormal pathway. The reverse occurs as if the pacing lead is present in the left ventricle, distal coronary sinus, or right ventricular septum, the paced QRS complex should show right bundle branch block pattern.
  Therefore, if the right ventricle is supposed to be the paced site and the ECG shows right bundle branch block, the lead may be pacing the right ventricular septum or it may have perforated the septum and is pacing the left ventricle unintentionally.

2- Chest X-ray Film: should be checked for lead position or lead fracture (figure 13-39).

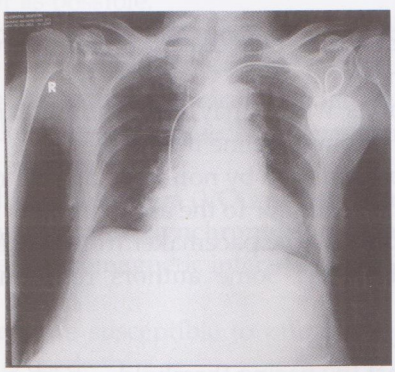


Figure 13-39: PA chest x-ray of a patient with permanent pacemaker inserted on the left side

Preoperative Patient Preparation:

1- Preoperative correction of s. K^+ is especially important in patients with pacemakers because the normal intracellular to extracellular K^+ ratio of 30: 1 maintains a resting membrane potential (RMP) of -90 mV; therefore,

a- Hyperkalemia may increase pacing: Acute hyperkalemia (i.e., acute increased extracellular K^+) by rapid K^+ administration, tissue ischemia, muscular fasciculations, or hypoventilation will decrease the usual ratio of 30: 1, causing a less negative RMP. Therefore, the preoperative pacemaker output setting can stimulate the myocardium to contract more easily. This increases the potential for ventricular tachycardia or ventricular fibrillation.

b- Hypokalemia may decrease pacing: acute hypokalemia (i.e., acute decreased extracellular K^+) by hyperventilation or intraoperative diuresis will increase the usual ratio of 30: 1, causing a more negative RMP and possible loss of pacing capture.

2- Automatic Implantable Cardioverter Defibrillator (AICD):

AICD can be discharged accidentally with electrocautery or other electrical signals generated by surgical equipment. Therefore, if the patient has an AICD, it should be **turned off preoperatively** and **turned back on in the postanesthetic care unit.**

3- Equipment and drugs for cardiopulmonary resuscitation should be prepared to be ready in case of pacemaker failure such as
- atropine and isoprenaline to treat bradycardia and heart block,
- lignocaine and defibrillator to treat ventricular arrhythmias.

Intraoperative Management:

Monitoring:

1. ECG monitor: should be continuously applied. The **"artifact filter"** on the ECG monitor should be **disabled** in order to detect the pacing spikes. During electrocautery, the ECG monitor is frequently useless due to interference. The best monitor available to detect if inhibition of the pacemaker is taking place is **a hand on the pulse.**
2. Pulse oximetry.
3. Noninvasive blood pressure.
4. End-tidal CO_2.
5- Esophageal or rectal temperature monitoring.

In addition to more cardiovascular monitors such as, invasive blood pressure (very important to detect pacemaker failure), central venous pressure, pulmonary artery pressure, cardiac output measurement, and transesophageal echocardiography.

Both central venous and pulmonary artery catheters have a potential for **dislodging the pacing electrode** particularly if the pacemaker has recently been inserted (< 2 weeks duration). However, if they are indicated, they should be used or alternative monitors of cardiac output measurement or the use of femoral vein for central venous access should be considered.

Anesthetic Techniques (Choice of Anesthesia):

Generally, the type of anesthesia and drugs used have a little influence on the pacemaker function.

A) Regional Anesthesia:

It can be used without interfering with the pacemaker function, but care should be taken if anticoagulants have been used.

B) General Anesthesia:

Induction:

- **I.v. agents** will **not affect** the pacing threshold except **etomidate** which may cause **myoclonus** which may produce myopotential interference.
- **Succinylcholine** causes fasciculations which may inhibit unipolar pacemakers due to myopotential interference; therefore, - avoid use of succinylcholine if possible.
  - perform defasciculation by non-depolarizing muscle relaxants.
  - reprogram the generator to the asynchronous mode or decrease the R wave sensitivity to prevent the pacemaker from sensing or receiving the myopotentials.

Generally, succinylcholine is used safely. Some authors recommend its usage after 4-6 weeks of electrode insertion.

Maintenance:

- **Inhalational** anesthetics do **not affect** the pacing threshold.

- N_2O is better **avoided** especially in a patient with a recently implanted pacemaker because N_2O could cause pacemaker malfunction by **increasing gas in the prepectoral pacemaker pocket.** Despite air evacuation with an antibiotic solution before closure of the prepectoral pocket, some air remains entrapped in the pocket (this small amount of air should have no clinical significance). When N_2O is used for general anesthesia, expansion of the gas in the prepectoral pocket may occur and cause loss of anodal contact and pacing system malfunction.
- **The use of drugs that suppress the AV or SA node (such as potent opioids or dexmedetomidine)** can abolish any underlying rhythm that might be present and render the patient truly pacemaker dependent.
- **Mechanical ventilation:**
  - **Avoid hyperventilation** because it causes hypocapnia and respiratory alkalosis with resultant **hypokalemia** which may necessitate increasing the energy output for pacing and capture.
  - **Programmable pacemakers with a rate-responsive function,** based on calculation of the ventilatory minute volume may induce tachycardia in patients who are subjected to hyperventilation during general anesthesia e.g., in neurosurgery. Therefore, the pacemaker should be reprogrammed to exclude the rate-responsive function with the use of an external programming device.

Intraoperative Complications:

1- Intraoperative Hypokalemia or Intraoperative Class I Antiarrhythmic Drugs: need to increase the energy output for pacing and capture.

2- Myopotential Interference:

It can cause inhibition of the pacemaker generator because they are falsely interpreted by the pacemaker as intrinsic R waves. This occurs with the types which sense the ventricles.

For example, - fasciculations of succinylcholine,
- myoclonus action of etomidate,
- postoperative shivering,

and - seizures.

Therefore, this problem can be prevented by reprogramming the pacemaker to an asynchronous mode or decreasing R wave sensitivity.

3- Electromagnetic Interference:

The pacemaker may pick up electric signals from any source of electromagnetic interference close to the patient e.g., surgical diathermy, magnetic resonance imaging (MRI), and defibrillator. This may shut off the unit or cause rapid pacing. It also possibly causes R on T phenomenon with inducing ventricular fibrillation.

Nowadays: - Good shielded pacemakers are available.
- New pacemakers are now designed such that, external electrical fields will change the pacemaker rhythm to an asynchronous mode rather than shut off the unit or cause VF.

a- Intraoperative Use of Defibrillators e.g., for VF, the following precautions should be taken during which:

- **The paddles should not be placed directly over the pulse generator.**
- **An acute increase in the stimulation threshold** may follow external defibrillation. This causes **loss of capture** and needs prompt insertion of a transvenous pacemaker.
- They may cause **endocardial burns and fibrosis** at the electrode-endocardial interface; therefore, increase the stimulation threshold and emphasize the need to administer the lowest effective dose of electrical energy by the defibrillator as possible.
- The pacemaker function should be checked following defibrillation.

b- Electrocautery:

It may cause **pacemaker failure** because the electrical artifact is sensed as an intrinsic myocardial potential (R wave) by the pacemaker. The response of pacemaker to the electrocautery is different according to the type of the pacemaker as follows:

- **Asynchronous non-programmable pacemakers** (VOO or AOO) are **not affected** by electrocautery.
- **Ventricular-inhibited non-programmable synchronous pacemakers** (VVI) are either completely inhibited (in the old models) by the electromagnetic interference or converted to asynchronous mode (in the new models).
- **Multi-programmable pacemakers** are susceptible to random reprogramming with electromagnetic interference especially if a magnet is used.

Electrocautery can also cause **myocardial burns and** may induce **ventricular fibrillation**; if the cautery comes in contact with a break in the insulation of the electrode, it may cauterize the myocardium at the tip of the electrode.

Precautions with Electrocautery:

1- Use **a bipolar** electrocautery as it is safe with the pacemakers. If a mono-polar forceps is used, a **pure cut is better** than blend or coagulation.

2- Use electrocautery in **short bursts** (1-second burst every 10 seconds) to prevent repetitive asystolic periods.

3- Set the electrocautery **current at the lowest functional level.**

4- **The ground plate** should be placed as close to the operative site as possible and as **far from the pacemaker generator** as possible (never have the generator between the ground plate and the site of cauterization).

5- The electrocautery **should not be used within 15 cm of the generator.**

6- Change **the pacemaker mode to asynchronous**:

• If a ventricular inhibited non-programmable synchronous-VVI pacemaker (old models) is used (inhibited by the electromagnetic interference), **a high-powered magnet** should be applied over the pacemaker generator to convert the pacemaker to an asynchronous fixed rate mode, but not all pacemakers have the same response to magnet (see above the response to magnet).

• If the pacemaker is multi-programmable, it should be reprogrammed preoperatively to an asynchronous mode or a programmer device should be in hand intraoperatively that can immediately reprogram the pacemaker generator to the synchronous or asynchronous modes according to the requirements.

7- If intraoperative pacemaker failure occurs, an **emergency transcutaneous pacemaker** (physio-control Quick pace) and atropine i.v. or ***isoprenaline infusion*** should be readily available.

8- **Cardiopulmonary resuscitation measures (equipment and drugs)** should be readily available.

c- Lithotripsy (Extracorporeal Shock Wave Therapy "ESWL")

• Generally, ESWL is no longer a contraindication for patients with pacemakers. The only exception to this general statement is the abdominally placed pacemaker generators that are used for epicardial pacing because these generators are in the blast path of the shock wave. Such patients should not be treated with ESWL. However, most transvenous pacemaker generators are placed in a pectoral location that is at a safe distance from the blast path.

• Some authors allow pacemakers to be used with ESWL under special precautions:

1. **Shock waves** should be of **low energy** initially (< 16 kV) then the energy level is **gradually increased** while the pacemaker function is carefully monitored.
2. The lithotriptor should be **at least 12 cm away from the pacemaker**.
3. Change the pacemaker mode as:
   - **DDD or atrial pacing** pacemakers are more sensitive to shock waves; so, they should be either:
     - Programmed to the ventricular pacing mode.
     or - Converted into the **asynchronous** mode.
   - **Multi-programmable** pacemakers can be malfunctioned by the shock waves; so, a **programmer** should be available in the lithotripsy suite.
4. **Emergency transcutaneous pacing** should be available in case the pacemaker becomes permanently damaged.

d- Electro-Convulsive Therapy (ECT):

It requires a non-sensing asynchronous mode to avoid sensing of seizures or succinylcholine fasciculations.

e- Electrical Peripheral Nerve Stimulators or Transcutaneous Electrical Nerve Stimulators (TENS):

They should be kept at least 12 cm from the pacemaker.

Postoperative Management:

It should be in the intensive care unit with backup pacing capability and cardioverter-defibrillator equipment. Special care is taken to:

- **Reevaluation of the pacemaker function** should be performed.
- Avoid **postoperative shivering** as it may cause myopotentials which may be misinterpreted by pacemakers as intrinsic myocardial potentials causing inhibition of the pacemaker.
- Patients with **AICD** turned off preoperatively should be **turned back on postoperatively.**

B) Anesthetic Management for Implantation of Pacemaker

Preoperative Management:

Preoperative Evaluation:

1- Assess the **cause of insertion** of the pacemaker e.g., heart block.

2- Assess **coexisting diseases** e.g., myocardial infarction, congestive heart failure and cardiac arrhythmias.

3- Assess for **adequate perfusion** before pacemaker implantation e.g., blood pressure and level of consciousness.

4- Preoperative **investigations** are indicated as before.

Preoperative Preparation:

1- **Equipment and drugs for cardiopulmonary resuscitation** as well as **external defibrillator** should be prepared to be ready in case of pacemaker failure such as:

- atropine and isoprenaline to treat bradycardia and heart block
- lignocaine and defibrillator to treat ventricular arrhythmias.

2- **Premedications**: **Light sedation** e.g., midazolam i.v. is usually used. **Avoid heavy sedation** because it may cause cardiopulmonary depression especially in these patients requiring the pacemakers as they are elderly and have cardiac diseases.

Intraoperative Management:

Monitoring: The same monitors are applied as during anesthesia of a patient with already implanted pacemaker (see above).

Anesthetic Techniques (Choice of Anesthesia):

a- Local Anesthesia (with sedation)

It is more preferable. **Small doses of short acting sedatives** are titrated to supplement local anesthesia such as thiopentone 25 mg increments, fentanyl 25 µg increments, midazolam 0.5 mg increments, or diazepam 1-2 mg increments. **O_2 mask** is applied to avoid hypoxia from sedation. **Hypoventilation** should **be avoided** by reminding the patient to take deep breaths intermittently.

b- Regional Anesthesia:

Combined **interscalene cervical plexus block** with **2nd, 3rd and 4th intercostal nerve block** is usually used. They provide satisfactory surgical anesthesia for implantation of the pacemaker without the need for large doses of local anesthetics or narcotic analgesia.

Both **local and regional techniques provide advantages** of patient's cooperation as the patient can be requested to: • cough to check for the possibility of electrode dislodgment,
or • breathe deeply to test diaphragmatic pacing.

c- Light General Anesthesia:

It is **better avoided** because patients with symptomatic heart block when given general anesthesia may develop cardiac standstill, ventricular tachycardia or ventricular fibrillation.

If complete heart block suddenly develops after induction of general anesthesia, isoprenaline infusion should be given. Recently, an external transcutaneous pacemaker (physio-control Quick-Pace) has become available. It may be used in emergency situations especially during anesthesia.

Postoperative Management:

A) Close Observation of the Patients is required for Detection of:

1- Complications Related to the Placement of the Pacemaker: such as thrombophlebitis, arterial puncture and hematoma, pneumothorax, cardiac perforation and tamponade, or infection at the site of the insertion.

Therefore, insertion of the pacemaker should be done by an experienced physician under aseptic conditions especially with intravenous and trans-thoracic types.

2- Complications Related to the Electrode:

Electrode disconnection and dislodgement may occur especially with the transvenous endocardial leads due to muscle movement, mechanical ventilation, or pulmonary artery catheter.

Therefore, patient transposition and transportation must be done with care to avoid this complication. Some recent types of pulmonary artery catheter contain an intracardiac pacemaker lead.

3- Induction of Arrhythmias:

With the fixed rate pacemaker i.e., asynchronous, the pacing stimulus may occur during the vulnerable T-wave period and **induce ventricular fibrillation**. This risk is very rare because the output of the

pacemaker is very small, except if there is a risk factor as acid-base or electrolyte disturbance, hypoxia, drug-induced complication as digitalis toxicity or catecholamines.

Therefore, ECG monitor is essential if there is a risk of ventricular fibrillation.

4- Complications Related to Traction:

Sometimes, it is necessary to remove the pacing electrode due to malfunction; the majority can be pulled out by gentle traction, but sometimes the pacemaker becomes adherent to the cardiac muscle. This may necessitate forceful prolonged traction which can cause:

- Arrhythmias as ventricular tachycardia or fibrillation.
- Shock due to invagination of the right ventricular wall into the tricuspid valve.
- Tear of the right side of the heart.

B) Advise the Patient to Avoid the Electromagnetic Sources of Interference affecting the function of a synchronous (demand) pacemaker such as:

- **Magnetic Resonant Imaging (MRI):** It is **absolutely contraindicated** by most generator manufacturers as deaths have been reported because it causes pacing inhibition or rapid pacing.
  If MRI is absolutely indicated, the pacemaker should be programmed to its lowest voltage output or pulse width or to OOO mode (provided that the patient has an adequate underlying rhythm).
- **Microwave oven:** Patients with old type pacemakers should not approach within 3 feet of an operating microwave oven. However, a modern pacemaker system can easily reject the interference.
- **Electric razor:** It should be avoided on the skin area over the implant site.
- **Telephone transformer:** It is contraindicated.
- **Power transmission lines:** High voltage electric fields should be avoided.
- **Cellular phones**: Analog cellular phones are safe, but digital cellular phones should not be placed over the pacemaker.
- **Radiation therapy** that can damage the pacemaker; therefore, appropriate shielding of the pulse generator is needed during radiation therapy.

The Physical Principles, Components, Pacemaker Identification, Types of Pacemaker, and Methods of Implantation of the Pacemaker are discussed in the chapter of "Basic Physics for Anesthesia & Intensive Care".

Automatic Implantable Cardioverter Defibrillator (AICD)

It was approved by the FDA in 1985.

Indications

1- Hemodynamically significant sustained ventricular tachycardia (VT).
2- Hemodynamically significant sustained ventricular fibrillation (VF).
Both are especially indicated when:

- They are not responding, or in cases with a contraindication to drug therapy or dysrhythmias surgery.
- They are not transient.
- They are not very excessive.
- They are associated with syncopal attacks.

3- Cardiac arrest resulting from VT/VF not resulting from a transient or reversible cause.
4- Post-myocardial infarction patients with ejection fraction less than 30%.
5- Cardiomyopathy of any cause (such as hypertrophic or dilated) with history of VT or VF and with ejection fraction $\leq$ 35%.
6- Awaiting heart transplant.
7- Long and short QT syndrome.
8- Brugada syndrome (right bundle branch block, and ST segment elevation in V_1 to V_3).
9- Arrhythmogenic right ventricular dysplasia.

Contraindications

1- Reversible etiologies of ventricular dysrhythmias such as:

- Drug toxicity: digitalis, quinidine, or phenothiazines.
- Electrolyte imbalance.
- Hypoxemia.
- Sepsis.

2- **Short, transient and unsustained** episodes of VT or VF e.g., those caused by acute myocardial infarction, electrocution or drowning.
3- **Frequent** and sustained episodes of **VT uncontrolled by drugs**, which will cause frequent discharges of the AICD and depletion of its battery.
4- Patients who require **a pacemaker (unipolar type);** AICD unit will not detect VF and may sense the pacing artifact as an R-wave.
5- Patients with: • **uncontrolled congestive heart failure,**
• medical illness with a **life expectancy of < 5-12 months,**
and • **psychological instability.**

Anesthetic Management

Anesthetic management with AICD is required either for patients undergoing placement of AICD or for patients with AICD undergoing non-cardiac procedure.

A) Anesthetic Management of a Patient Undergoing Placement of AICD

The procedure may be straightforward, when two venous wires (sensing and shocking) are positioned transvenously, or complex when the pacemaker is replaced or the coronary sinus is catheterized to gain access to the left ventricle muscle. Fluoroscopy is needed to guide the position of the leads with complete aseptic techniques to avoid infection of the prosthesis. During the procedure, VF is induced to test the device. If the device does not work, do not allow the heart to be stopped with VF for long where it must be treated. The patient needs to be sedated during this phase. After VF and shocking, the blood pressure may remain low for a short period where vasopressors may be needed

Preoperative Management:

Preoperative Evaluation: It is the same as the pacemaker evaluation (see above).

Preoperative Preparation:

1- Preoperative **correction** of:
• **Blood pressure:** by short-acting drugs or drugs that have a little effect on the heart rate; so that intraoperative evaluation of patient's arrhythmias is not impaired.
• Correction of **electrolyte** imbalance especially K^+ (by chronic diuretic therapy).
• Correction of **pulmonary status** such as chronic obstructive airway diseases by adequate hydration (keeping in mind possibility of congestive heart failure), controlling respiratory infections, chest physiotherapy, and bronchodilator therapy (potentially arrhythmogenic).
2- **Discontinuation of antiarrhythmic medication:** for 24-48 hours before surgery; so that induction of intraoperative dysrhythmias is facilitated. This is very important in assessing proper function of AICD intraoperatively (i.e., the dysrhythmias must be induced intraoperatively and the AICD counter-shock should terminate it).
3- Preparation of **emergency drugs** for resuscitation (already drawn up into syringes to save time if needed) e.g., atropine, adrenaline, $CaCl_2$, $NaHCO_3$, phenylephrine, nitroglycerin infusion, and electric cardioversion should be available in the operative room (both external and internal cardioversion).
4- **ECG monitoring** should be done **in the preoperative period** and **during patient transportation** to the operative room because the anti-arrhythmic drugs are stopped 24-48 hours preoperatively. Therefore, the patient becomes vulnerable for occurrence of arrhythmias.
5- **Premedications: Avoid heavy sedation** as the patient is very susceptible to ventricular arrhythmias and heavy sedation can cause hypoxia or hypercarbia. Therefore, midazolam is sufficient.

Intraoperative Management:

Monitoring is the same as that applied in pacemaker insertion.

Anesthetic Techniques:

Implantation of AICD is usually performed through either a subcostal or lateral thoracotomy incision. Implantation of AICD does not require cardiopulmonary bypass, but may be combined with revascularization operations.

Aim: • Avoid factors that increase arrhythmias such as hypoxia, hypercarbia, and postoperative pain.
• Avoid hemodynamic instability (i.e., hypotension).

Choice of Anesthesia:

The best is combined thoracic epidural analgesia and light general anesthesia. In some cases, light general anesthesia is enough.

a- Thoracic Epidural Analgesia:

• After monitors are applied, thoracic epidural analgesia is performed at T_7-T_9 interspace.

• After the thoracic epidural catheter is applied, general anesthesia is induced.

Advantages:

a- Intraoperative:

• It achieves a band of anesthesia which enables the patient to tolerate the endotracheal tube.

• It decreases the dose of general anesthetics and avoids the usage of opioids which can cause respiratory depression.

N.B.: **Chloroprocaine is used** intraoperatively. **Avoid lignocaine** as it may inhibit the ability to induce the patient's arrhythmias intraoperatively if systemic absorption of the drug occurs.

b- Postoperative: It should provide **analgesia** for at least 36-48 hours postoperatively.

• It decreases the adverse effects of postoperative pain such as tachycardia, hypertension, or myocardial ischemia (due to increased sympathetic tone), respiratory insufficiency, hypoxemia, and increased susceptibility to pulmonary infections (due to inhibition of deep breathing and coughing by pain).

• It allows minimal application of sedative drugs with their side effects.

• It improves chest physiotherapy.

• It allows early ambulation.

• It decreases adverse reactions of systemic analgesics e.g., opioids.

b- Light General Anesthesia:

Induction:

• Preoxygenation with 100 % O_2.

• Induction agents: midazolam and sufentanil.

• Intubation is done by vecuronium or cis-atracurium at the intubating dose.

Maintenance:

• N_2O: O_2 are used in a ratio of 6: 4. **O_2 is increased to 100 % before induction of the arrhythmia.**

• Volatile agents such as sevoflurane or opioids such as sufentanil are used in small doses.

• Nondepolarizing muscle relaxants: such as **vecuronium or cis-atracurium** are of choice.

Intraoperative Induction of Dysrhythmia:

It is done to assess the function of the AICD. Before induction of arrhythmias the following precautions should be performed:

• Give 100% O_2 to maximize O_2 delivery during episodes of VT or VF.

• Give midazolam to ensure amnesia.

If the AICD is functioning properly, it will cardiovert the patient to normal sinus rhythm during the next 10-15 seconds. If the AICD is not functioning properly and has failed to correct the patient's dysrhythmia, **electric cardioversion** should be applied by one of the following methods:

• **Internal** cardioversion through paddles applied directly to the myocardium. It is performed by the surgeon (about 20 joules).

• **External** cardioversion, if internal paddles can not be applied.

Recheck **arterial blood gases** and s. **electrolytes** (especially **s. K^+**) and **optimize pH.**

Sequences (and Complications) of Induction of Arrhythmias:

1- Hypotension:

It is the most common complication occurring **during induction of arrhythmia** by rapid pacing, because arrhythmias shorten the diastolic period. This impairs diastolic left ventricular filling. Once VF occurs, hypotension is due to lack of coordinated ventricular contraction.

It may also occur **after cardioversion**. It should be treated by phenylephrine 100 µg i.v. increments. To avoid myocardial ischemia also, arterial blood gases should be rechecked and managed.

2- Hypertension and tachycardia:

• Both can occur after cardioversion due to increased sympathetic outflow (although, there is no documentation in the literatures).

• Immediately, in the post-cardioversion period, both hypertension and tachycardia are not treated, but if they persist, they are treated with esmolol to avoid the increase in myocardial O_2 consumption.

3- ST-segment elevation and myocardial ischemia:

After a DC shock, an ST segment elevation may occur either due to:

• **Injury** from the DC shock. It is rare for myocardial damage to occur following internal or external counter shock.

• Myocardial ischemia especially with VF.

If ST-segment elevation persists for > 10 min, it should be **managed as myocardial ischemia** such as administration of **nitroglycerin and phenylephrine** to decrease the preload and ventricular wall tension

and maintain adequate perfusion pressure. If adequate perfusion pressure exists, there will be no need to utilize phenylephrine. If hypertension exists, nitroglycerin may not only improve the collateral blood flow to the ischemic myocardium, but may also decrease the accompanying elevated blood pressure.

Emergence:

The patient is either: - extubated in the operative room,
or - transferred intubated to the intensive care unit.

Postoperative Management:

The patient should be **in intensive care unit** until the AICD is checked and reactivated.

1- If the patient is transferred intubated, **ventilatory support** is indicated usually for 24 hours or more till the hemodynamic status becomes stable and criteria for extubation become fulfilled.

2- Proper control of **postoperative pain** is essential to avoid sympathetic stimulation and respiratory dysfunction. This is achieved by thoracic epidural analgesia (of choice) or careful titration of narcotics to avoid respiratory depression.

3- **Postoperative complications** should be detected and managed such as:

- Pulmonary dysfunction.
- Postoperative bleeding.
- Constrictive pericarditis.
- Pulmonary edema.
- Postoperative ventricular tachycardia.
- Lead fracture or dislodgement.
- Infection: is very common and is seen in up to 20% of patients. It mandates partial or complete removal of the system.

B) Anesthetic Management of a Patient with an AICD Undergoing Surgery:

Anesthetic Problems:

The same anesthetic principles as these applied for a patient with pacemaker are applied here.

Electromagnetic Interference (Effect of Electrocautery):

- **False discharge** of the AICD can occur with **electrocautery** or other electrical signals from surgical equipment because the AICD may interpret the electrical signals as ventricular fibrillation.
- It has been reported that electrocautery has **initiated a counter-shock sequence** by the AICD which **causes VT**.

Precautions with Electrocautery:

- It is necessary to **deactivate the AICD device with a ring magnet**, but actually the effect of magnet application, like pacemakers, gives **unpredictable effects with AICD** such as:
  - Most AICDs devices will temporary suspend tachyarrhythmia detection (and therefore therapy).
  - Some other devices can be permanently disabled by magnet placement for > 30 seconds.
  - Generally, **most devices are not affected**.
- **The same precautions** taken **with the pacemaker** are applied with AICD.

The Components, Physical Principles, Codes, and Potential Problems are discussed in chapter "Basic Physics for Anesthesia & Intensive Care".

Integrated Cardio-Pulmonary Function Capacity

These are a group of assessments that involve combining the assessment of the cardiac and pulmonary functions.

The following tests can assess cardiopulmonary functions, but with their limitations. Cardiopulmonary exercise testing is the only test that can assess the cardiopulmonary function in a great validity.

I) Preoperative Exercise Capacity

II) The Duke Activity Status Index: is discussed above.

III) Shuttle-Walk Test:

The subject can walk at a predetermined increasing speed between cones placed 10 meters apart. Interpretation of results is as follows:

- Achieving **< 250 meters** indicates maximum O_2 consumption of less than 10 mL/kg/min; it indicates **very high risk**.
- Achieving **between 250-450 meters** indicates **middle risk**.
- Achieving **> 450 meters** indicates maximum O_2 consumption of greater than 14 mL/kg/min; it indicates **low risk**.

• **Desaturation** on pulse oximetry of **greater than 4% during the test** indicates **increased risk**, as does **myocardial ischemia on Holter ECG** monitoring.

IV) 6-Minute Walk Test:

It is the maximum distance a patient can walk in 6 minutes.

V) Cardio-Pulmonary Exercise Testing "CPET":

It is the most sensitive test to detect the high risk patients after major surgery. The CPET involves computerized continuous analysis of gas exchange and ECG data during exercise. It is a non-invasive test. It is very important for patients with cardiac failure postoperatively to decrease postoperative morbidity and mortality. Myocardial ischemia and analysis of risk factors for coronary artery disease e.g., diabetes, hypertension, hyperlipidemia, smoking has no role in the perioperative evaluation and prediction of mortality and morbidity.

Technique of CPET:

• It consists of an exercise test with a progressive graded work rate and simultaneous breath-by-breath measurement at the mouth, of inspired and expired concentration of O_2 and CO_2, and inspiratory and expiratory gas flow; therefore, **O_2 uptake and CO_2 output, work rate in watts, minute and tidal volume, and flow-volume loops** are displayed continuously. In addition, a **12-lead ECG** is obtained at rest and continuously during exercise and in the recovery period.

• **A "zero watt" cycle ergometer** (a non-movable cycle) is the method of exercise used (figure 13-40). A "zero watt" means that the cycle performs a work to help the patient in doing exercise. The patient is performing no extrinsic work, but only performing intrinsic work (by his or her legs). The intrinsic work performed by the average patient is approximately 25 watts. A "zero watt" cycle ergometer has the following **advantages** over the treadmill:

1- It produces better isolation of lower limb musculature without affecting other muscles.
2- It produces less effects of movement artifact on the results.
3- There is greater safety because the subject is supported.
4- The workload can be varied in a step, incremental, or ramp manner.

These factors contribute to a more precise estimation of workload:

• Resuscitation equipment and drugs should be available.
• **During the first minute of the test**, **baseline** gas exchange **data** are collected.
• **Then for the next 3 minutes**, the patient is cycled against a zero watt extrinsic load;
for the next 6 minutes, the extrinsic load is increased progressively using a ramp protocol to achieve the predicted maximum work rate.

The duration of the test is usually less than 9-10 minutes especially in age over 60 years.

• **The test is stopped** if the ECG shows greater than 2 mm ST depression 60 msec after the J-point in any lead or if the patient becomes distressed.

Data Obtained From the CPET:

The CPET is done to **evaluate the functional capacity of the heart and lungs** which is the main risk factor for postoperative mortality and morbidity. Myocardial ischemia is now not the risk factor for morbidity and mortality. This is done by:

1- The Anaerobic Threshold (AT):

Definition: It is **the point of O_2 uptake** where anaerobic metabolism starts to supplement the aerobic metabolism with ATP (adenosine triphosphate). At this point, the aerobic metabolism is insufficient. It is used to define the grade of cardiac failure.

Method: The anaerobic threshold can be obtained by plotting CO_2 production ($\dot{V}CO_2$) against O_2 consumption ($\dot{V}O_2$) as a V-slope plot (figure 13-41).

At rest a subject will consume about 250 mL/min O_2 and produce 200 mL/min CO_2 giving a respiratory quotient (CO_2/O_2) of 0.8. With increasing exercise, the O_2 consumption ($\dot{V}O_2$) will increase in line with CO_2 ($\dot{V}CO_2$) until the subject switches to anaerobic metabolism, when CO_2 production will start to rise more quickly than O_2 consumption and the respiratory quotient will exceed 1.0. The AT can be determined from the graph at the inflection point on the V-slope plot.

2- The O_2 Consumption:

It is 3.5 mL/kg/min at rest. It increases up to 6-7 mL/kg/min with surgical stress at rest. It increases more with mobilization or presence of complications.



Figure 13-40: Cardio-pulmonary exercise testing

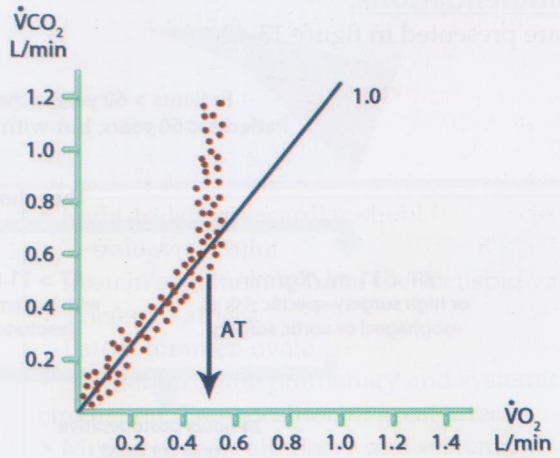


Figure 13-41: V-slope plot

3- Cardiovascular Response to Exercise.
4- Ventilatory Response to Exercise.
5- Ventilation/Perfusion Response to Exercise.
6- Metabolic Responses to Exercise.

These data are recorded on 15 graphs.

Value:

- Patients with **AT < 11 mL/kg/min, $\dot{V}O_2$ maximum/m² of < 800 mL/min/m²** and having **evidence of myocardial ischemia** before reaching AT are **at a great risk** of cardiovascular death after doing major surgery and need **more intensive perioperative care**.
- Patients with myocardial ischemia after AT (11 mL/kg/min) are at increased risk compared to those without myocardial ischemia.
- Patients with **$\dot{V}O_2$ maximum/m² of > 1100 mL/min/m²** very rarely develop cardiovascular complications.
- Using CPET data, cardiac failure is classified into 5 groups according to AT. They range from no heart failure to significant heart failure (between 14 mL/kg/min to 8 mL/kg/min)

Advantages of CPET:

1- It is proved that using CPET data is better than using age, history, or physical examination as a detriment for heart failure and prediction of morbidity and mortality. **Cardiovascular mortality is associated with AT less 11 mL/kg/min.**

2- It defines cardiac failure even at subclinical levels, as well as identifying myocardial ischemia preoperatively.

3- It is non-invasive, objective, and is performed on all patients, including outpatients.

4- It is less time consuming and is with less cost.

5- It will accurately determine the severity of cardiac functional limitation prior to major surgery.

Disadvantages of ECG Stress Test:

1- It is a test for myocardial ischemia not heart failure which is the major problem. The recent researches have proved that heart failure is more predictive than myocardial ischemia in detection of morbidity and mortality.

2- It is a **less accurate test:**

32% of patients with myocardial ischemia will not have a positive exercise ECG test.

23% of patients may have false positive results (without having myocardial ischemia and so their surgeries may be delayed and are likely to have more investigations for a disease they do not have).

3- It may not be interpreted in spite of presence of ischemia as in patients with left bundle branch block, paced rhythm, or conduction abnormalities. This is not a problem in CPET as gas analysis can be done even without ECG test.

Disadvantages of Other Screening Tests: as dipyridamole-thallium scintigraphy or dobutamine-stress echocardiography): these tests may not diagnose presence of heart failure because 40-50% of patients with heart failure may have a normal ejection fraction.

Recommendations:

They are presented in figure 13-42.

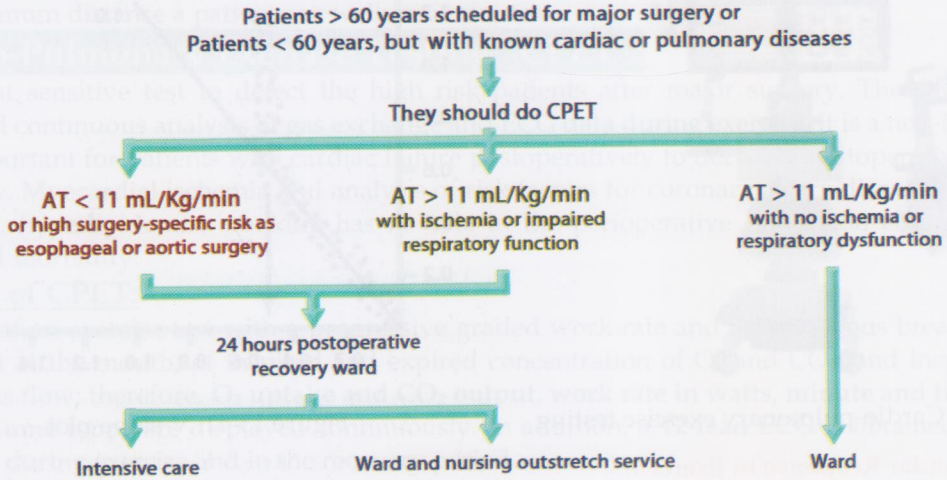


Figure 13-42: Recommendations of CPET

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CONGENITAL CARDIOVASCULAR DISEASES

14

- Classification
- Anesthetic management
  - Preoperative management
  - Aim during anesthesia
- Obstructive lesions
  - Congenital aortic stenosis
  - Coarctation of the aorta
  - Interrupted aortic arch anomaly
  - Pulmonary atresia
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  - Secundum atrial septal defect
  - Primum atrial septal defect
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  - Patent ductal arteriosus
  - Aorticopulmonary fenestration
- Right-to-left intracardiac shunt
  - Tetralogy of Fallot
  - Ebstein's malformation of the tricuspid valve
  - Tricuspid atresia
  - Patent foramen ovale
- Separation of the pulmonary and systemic circulation: Transposition of great arteries.
- Mixing of the pulmonary and systemic circulation
  - Hypoplastic left heart syndrome
  - Truncus arteriosus
  - Partial anomalous pulmonary venous return
  - Total anomalous pulmonary venous return
  - Double outlet right ventricle
- Mechanical obstruction of the trachea
  - Double aortic arch
  - Aberrant left pulmonary artery
  - Absent pulmonary valve

Congenital cardiovascular diseases represent 1% of all live births.

Classification: and the related clinical picture

I. Obstructive Lesions:

a. Left ventricle: They produce **clinical pictures of congestive heart failure.**

- Congenital aortic stenosis.
- Coarctation of the aorta.
- Interrupted aortic arch anomaly.

b. Right ventricle: They produce **clinical pictures of congestive heart failure and decreased pulmonary blood flow.**

- Pulmonary atresia.

II. Left to Right Intracardiac Shunt (Simple Shunts):

They produce **clinical picture of increased pulmonary blood flow.**

- Secundum atrial septal defect (Secundum ASD) (Ostium secundum).
- Primum atrial septal defect (Primum ASD) (Ostium Primum) (Endocardial cushion defect).
- Ventricular septal defect (VSD).
- Patent ductus arteriosus (PDA).
- Aorticopulmonary fenestration.

III. Right to Left Intracardiac Shunt:

They produce **clinical picture of decreased pulmonary blood flow.**

- Tetralogy of Fallot.
- Ebstein's malformation of tricuspid valve.
- Tricuspid atresia.
- Patent foramen ovale.
- Eisenmenger's syndrome.

IV. Separation of the Pulmonary and Systemic Circulation:

They produce **clinical picture of increased or decreased pulmonary blood flow.**

- Transposition of the great vessels.

V. Mixing of the Pulmonary and Systemic Circulation:

They produce **clinical picture of increased or decreased pulmonary blood flow.**

- Truncus arteriosus.
- Partial anomalous pulmonary venous return (some authors consider it group II).
- Total anomalous pulmonary venous return.
- Hypoplastic left heart syndrome.
- Double outlet right ventricle.
- Single ventricle or single atrium.

VI. Mechanical Obstruction of the Trachea:

- Double aortic arch.
- Aberrant left pulmonary artery.
- Absent pulmonary valve.

N.B.: **Cyanotic heart diseases** in the 1st year of life (or at birth) include groups **Ib, III, IV, and V**.

Anesthetic Management

Patients with congenital cardiovascular diseases undergoing surgical procedures are one of the following groups:

a- Patients who have undergone corrective cardiac surgery: They are considered normal, but a prophylactic antibiotic is essential against infective endocarditis.

b- Patients who had only palliative surgery.

c- Patients who have not yet undergone any cardiac surgery.

d- Patients who have inoperable conditions and may be awaiting cardiac transplantation.

b, c, and d need special anesthetic management according to the disease.

Preoperative Management:

A. Detection of Congenital Cardiovascular Disease:

Clinical Pictures:

Many are **asymptomatic up to adulthood**, but others show:

1- Failure to gain weight in infants or slow physical development in children and easy fatigability.

2- The congenital heart diseases produce clinical pictures according to the pulmonary blood flow. Some congenital cardiovascular diseases produce increased pulmonary blood flow while other diseases produce decreased pulmonary blood flow.

a- Clinical picture of **increased pulmonary blood flow:** Pulmonary congestion causes:

- recurrent chest infection,
- later on, pulmonary hypertension, and
- finally congestive heart failure with exertional dyspnea, cyanosis, syncope, anginal attacks, and decreased exercise tolerance.

b- Clinical picture of **decreased pulmonary blood flow:** Pulmonary oligemia causes arterial hypoxemia.

- Cyanosis, tachypnea especially on feeding, and clubbing of digits.

3- Heart murmurs (see later).

4- Associated chromosomal abnormalities:

10% of congenital cardiovascular diseases are associated with chromosomal abnormalities while the remaining 90% of congenital cardiovascular diseases are due to multi-factors interactions such as rubella, ethanol abuse, lithium, and maternal diabetes mellitus.

Examples for the chromosomal abnormalities:

- 2/3 of patients with trisomy 21 are associated with congenital cardiovascular diseases.
- 1/3 of patients with karyotypic abnormalities such as trisomy 13 and trisomy 18 and patients with Turner's syndrome are associated with chromosomal abnormalities.
- CATCH-22 is a widely used acronym that indicates **C**ardiac defects, **A**bnormal facies, **T**hymic hypoplasia, **C**left palate, and **H**ypocalcemia. It is due to a defect in chromosome **22**.

Investigations:

1. Transthoracic or transesophageal echocardiography *is the initial diagnosis. It is done if:*

- a congenital cardiovascular disease is suspected by the above clinical picture or
- there are associated congenital anomalies.

2. **Doppler ultrasonography:** has more advantages than echo. It provides further information in demonstrating **valvular** dysfunction and **septal defects**.
3. **Fetal cardiac ultrasonography** can allow prenatal diagnosis of congenital cardiovascular diseases.
4. **Computed tomography (CT scan)** has more advantages than echo.
It provides further information in demonstrating anomalies of the **great vessels**.
5. **Magnetic resonance images (MRI)** has more advantages than CT scan. It offers a better resolution without the need for radio-opaque contrast media.
6. **Cardiac catheterization and selective angio-cardiography** are the **most definitive** diagnostic techniques available.
7. ECG shows: • ventricular or atrial enlargement.
• associated arrhythmias (very rare).
8. **Chest X-ray** shows: • pulmonary congestion and prominent pulmonary arteries, if pulmonary blood flow is increased.
• pulmonary oligemia, if pulmonary blood flow is decreased.
• chamber enlargement.
• characteristic shape as boot-shaped heart of tetralogy of Fallot.

B. Detection of General Complications and Problems: in all congenital cardiovascular diseases.

1. **Infective endocarditis:** Patients should receive prophylactic antibiotics before any dental or surgical procedure.
2. **Hyperuricemia** (i.e., increased uric acid): due to increased urate reabsorption secondary to renal hypoperfusion. It may progress to renal impairment.
3. **Dysrhythmias.**
4. **Complete heart block.**

Monitoring

Besides the **standard monitors**, **invasive blood pressure** and **central venous pressure** are essential during anesthesia.

Aim during Anesthesia

The aim during anesthesia is to correct the imbalance between systemic and pulmonary blood flow.
For example,

- **Left to right shunts** are associated with increased pulmonary blood flow; therefore, the primary aim during anesthesia is to increase the pulmonary vascular resistance and to decrease the systemic vascular resistance. This will correct the increased pulmonary blood flow and produce balance of the ratio between the pulmonary and systemic blood flow.
- **Right to left shunts** are associated with decreased pulmonary blood flow (with hypoxia); therefore, the primary aim during anesthesia is to increase the systemic vascular resistance and to decrease the pulmonary vascular resistance. This will correct the decreased pulmonary blood flow and produce balance of the ratio between the pulmonary and systemic blood flow.

General Principles and Aim during Anesthesia of Congenital Cardiovascular Diseases:

- Meticulous exclusion of air bubbles or clots from tubing of i.v. fluids is required to avoid paradoxical air embolism into the cerebral or coronary circulation, regardless of the direction of the blood flow.
- Avoid dehydration and follow the preoperative fasting guidelines.
- Avoid myocardial depression.
- Maintain sinus rhythm whenever possible.
- Provide sedation and close monitoring.
- Antibiotic prophylaxis against infective endocarditis is essential.

Events controlling systemic and pulmonary vascular resistance:

A) Events that Decrease Systemic Vascular Resistance:

- Deep anesthesia.
- Hypoxemia.
- Severe hypercarbia.
- Vasodilators or ganglion blockers.
- Volatile agents.

- Histamine releasing drugs
- α-blockers.
- β-agonists.
- Ca^{++} channel blockers.
- Phosphodiesterase III inhibitors.

B) Events that Increase Pulmonary Vascular Resistance:

- Light anesthesia.
- Sympathetic activation.
- Administration of N_2O.
- Alveolar hypoxemia (i.e., low inspired O_2 concentration).
- Hypercapnia.
- Acidosis.
- High lung volumes or pressures (tend to collapse pulmonary capillaries) such as mechanical ventilation with high airway pressures or positive end expiratory pressure (PEEP).
- Opening of the chest causes loss of negative intrapleural pressure.
- Low lung volumes with atelectasis (tend to collapse pulmonary blood vessels).
- Hypothermia.

Both "A" and "B" events are indicated in left to right shunts and other congenital cardiovascular diseases with **increased pulmonary blood flow** and should be **avoided** in **right to left shunts and** other congenital cardiovascular diseases with **decreased pulmonary blood flow.**

C) Events that Increase Systemic Vascular Resistance:

- Light anesthesia.
- Sympathetic activation.
- α-agonists.
- Physical manipulations (compression of the femoral arteries by flexing the hips of infants and small children i.e., squatting).

D) Events that Decrease Pulmonary Vascular Resistance:

- Administration of high O_2 concentration (FiO_2).

Both "C" and "D" events are indicated in right to left shunts and other congenital cardiovascular diseases with **decreased pulmonary blood flow** and should be **avoided in left to right shunts** and other congenital cardiovascular diseases with **increased pulmonary blood flow**

I. Obstructive Lesions

1- Congenital Aortic Stenosis

There are 3 types: (differentiated by cardiac catheterization).

a) Valvular (Bicuspid Aortic Valve):

Clinical Picture:

The deformed bicuspid valve is not stenotic at birth, but with time, thickening and calcification of the leaflets (usually not apparent before 15 years of age) occur with resulting immobility of leaflets. Therefore, it is asymptomatic until adulthood. Angina, syncope, and congestive heart failure are common presentations

The principles of anesthetic management are nearly the same as **rheumatic aortic stenosis** (see before).

b) Sub-valvular:

The principles of anesthetic management are nearly the same as **hypertrophic cardiomyopathy** (see before).

c) Supra-valvular:

The clinical picture and principles of anesthetic management are nearly the same as **rheumatic aortic stenosis** (see before). These patients have characteristic appearance:

- Prominent facial bones with rounded forehead.
- Pursed upper lip.
- Strabismus.
- Inguinal hernia.
- Dental abnormalities.
- Moderate mental retardation.

• Unequal blood pressure in the upper extremities depending on how the high velocity jet stream of blood ejected through the stenotic aortic valve strikes the innominate artery.

Complications and Investigations: are discussed above.

Treatment:

• Surgical correction by widening the lumen of the aorta with an artificial patch.
• Antibiotics against infective endocarditis.

2- Coarctation of the Aorta

It is discussed later in chapter "Anesthesia and Vascular Surgery".

3- Interrupted Aortic Arch Anomaly

It is **complete atresia of the aortic arch**. There are 3 types:

Type A (43%): The atresia lies between the left subclavian artery and the aortic isthmus.
Type B (53%): The atresia lies between the left carotid and the left subclavian arteries.
Type C (4%): The atresia lies between the right and left carotid arteries.

DiGeorge syndrome is present in 50% of the patients with interrupted aortic arch anomaly.
Ventricular septal defect is present in most patients.

Pathophysiology:

Due to the atresia, no blood flow can go to the descending aorta unless a patent ductus arteriosus exists where patent ductus arteriosus carries blood from the pulmonary artery to the aorta. If the ductus cannot provide adequate perfusion to the lower body due to its closure, severe metabolic acidosis and renal insufficiency occur.

With a ventricular septal defect, most of the cardiac output will be directed into the pulmonary vascular bed as the ductus closes. These patients are at risk of a profound low cardiac output syndrome. Therefore, ductal patency is essential to avoid death.

Investigations:

Two-dimensional echocardiography is diagnostic. Other investigations are discussed above.

Treatment:

1- Prostaglandin E_1 (PG E_1):

Action: It delays the natural closure of the ductus and improves arterial oxygenation. It is essential for the neonate's life. Due to its long half-life, discontinuation of the drip will not acutely cause ductal closure in case of inadvertent stoppage.

Side effects: Fever, hypotension, dysrhythmias, seizures, flushing, peripheral edema, and decreased platelet aggregation. Apnea in premature infant requires intubation and mechanical ventilation.

Dose: Titration of 0.05-0.1 µg/kg/min.

2- Surgical correction.

4- Pulmonary Stenosis

There are 3 types:

a) Valvular 90%: is usually isolated.

b) Subvalvular (infundibular): is usually associated with ventricular septal defect.

c) Supraventricular: is usually associated with other congenital cardiac abnormalities such as atrial septal defects, ventricular septal defects, patent ductus arteriosus, tetralogy of Fallot; or associated with Williams syndrome (infantile hypocalcemia and mental retardation).

Pathophysiology:

Pulmonary valve stenosis obstructs right ventricular outflow which in turn decreases pulmonary blood flow and causes concentric right ventricular hypertrophy. Later on, right ventricular hypertrophy and right ventricular failure (congestive heart failure) may occur.

1- Mild to Moderate Pulmonary Stenosis:

It is asymptomatic.

2- Severe Pulmonary Stenosis: (the pressure gradient across the valve is > 50 mm Hg by catheterization) produces the following clinical picture especially in neonates:

• Decreased pulmonary blood flow symptoms as cyanosis.

• Congestive heart failure symptoms such as exertional dyspnea, cyanosis, syncope, and anginal attacks.
• Sudden death due to right ventricular infarction.
• Systolic ejection murmur: It is best heard at the 2nd left intercostal space. The intensity and the duration of the murmur parallel the severity of the stenosis.

Treatment:

1. Surgical correction:
   a. Valvular : valvotomy by cardiopulmonary bypass.
   b. Infundibular: resection of excess ventricular muscle.
2. Catheter balloon valvuloplasty.

Anesthetic Management:

Aims: Congenital pulmonary stenosis is associated **with decreased pulmonary blood;** therefore, the aim during anesthesia is as follows:

1- **General aim and principles:** as above such as avoiding hypovolemia and dehydration.

2- **Advocate** events that **increase systemic vascular resistance** (such as light anesthesia or treatment of hypotension by α-agonists and other sympathomimetics) and that **decrease pulmonary vascular resistance** (administration of high O_2 concentration).

3- **Avoid** events that **decrease systemic vascular resistance** (such as deep anesthesia, hypoxemia, hypercarbia, hypotensive agents i.e., vasodilators, volatiles, histamine releasing drugs, and α-blockers) and that **increase pulmonary vascular resistance** (such as administration of N_2O, high lung volumes and pressures). Mechanical ventilation slightly increases pulmonary vascular resistance, but usually has no clinical effect.

4- **Keep the heart rate at a normal rate** because cardiac output depends primarily on the heart rate (as stroke volume can not be increased due to the presence of pulmonary stenosis), but avoid excessive increase in the heart rate or contractility as this causes undesirable effects on ventricular filling. Therefore, increased heart rate should be treated by propranolol or esmolol.

N.B.: These patients are difficult to resuscitate by external cardiac compression which fails to force blood across the stenotic valve; therefore, an electrical defibrillator should always be available.

The aim during anesthesia is nearly similar to the anesthetic management of any stenotic valve lesion (see before in the chapter of "Cardiovascular Disease").

II. Left to Right Intracardiac Shunt (Simple Shunts)

They include:

1. Secundum atrial septal defect.
2. Primum atrial septal defect (Endocardial cushion defect).
3. Ventricular septal defect.
4. Patent ductus arteriosus.
5. Aorticopulmonary fenestration.

Pathophysiology

Simple shunts are isolated abnormal communications between the right and left sides of the heart; therefore, blood flows across which from the left to the right side. This increases blood flow through the right heart leading to **increasing the pulmonary blood flow**. This is because the pressures are normally higher on the left side.

The right ventricle may also be subjected to the higher left sided pressure, according to the site of the shunt. Right ventricular afterload is normally 1/6 that of the left ventricle; therefore, even small left to right pressure gradients can produce large increases in pulmonary blood flow.

Calculation Q_P: Q_S:

• Shunting is defined generally as the process whereby venous return into one circulatory system is recirculated through the arterial outflow of the same circulatory system. It is either:

a- Left to right shunt: in which flow of blood from the pulmonary venous atrium (left atrium) to the pulmonary artery produces recirculation of pulmonary venous blood.

b- Right to left shunt: in which flow of blood from the systemic venous atrium (right atrium) to the aorta produces recirculation of systemic venous blood.

- **Effective Blood Flow:** is the quantity of venous blood from one circulatory system reaching the arterial system of the other circulatory system. It is either:

  a- Effective pulmonary blood flow: It is the volume of systemic venous blood reaching the pulmonary circulation.

  b- Effective systemic blood flow: It is the volume of pulmonary venous blood reaching the systemic circulation.

Both effective pulmonary and effective systemic blood flows are the flows necessary to maintain life and they are always equal, no matter how complex the lesions are.

Effective blood flow is usually the result of a normal pathway through the heart, but it may occur as the result of an anatomic right to left or left to right shunt.

- **Total Pulmonary Blood Flow (Q_P):** is the sum of effective pulmonary blood flow and recirculated pulmonary blood flow (i.e., normal pathway flow and left to right shunt flow).
- **Total Systemic Blood Flow (Q_S):** is the sum of effective systemic blood flow and recirculated systemic blood flow (i.e., normal pathway flow and right to left shunt flow).

Both Q_P and Q_s do not have to be equal.

Because Q_s (systemic cardiac output) tends to remain constant to supply end organs, a physiological left to right shunt (pulmonary recirculation) causes volume overload, while a physiological right to left shunt (systemic recirculation) allows Q_s to be maintained at the expense of arterial O_2 saturation (SaO_2) (figure 14- 1).

$\frac{Q_P}{Q_s}$ ratio is the ratio of total pulmonary blood flow to systemic blood flow.

$$\frac{Q_P}{Q_s} = \frac{SaO_2 \; S_{SVC}O_2}{S_{PV}O_2 \; S_{PA}O_2}$$

Where: SaO_2 = O_2 saturation of arterial blood.
$S_{SVC}O_2$ = O_2 saturation of superior vena cava.
$S_{PV}O_2$ = O_2 saturation of pulmonary vein that can be assumed to be 98% in the absence of significant pulmonary disease.
$S_{PA}O_2$ = O_2 saturation of pulmonary artery.

A ratio > 1 indicates a left to right shunt.
A ratio < 1 indicates a right to left shunt.
A ratio = 1 indicates either no shunt or bidirectional shunt of opposing magnitudes.

N.B.: Calculation of Q_P/Q_s is greatly simplified when it is made while using low inspired O_2 concentrations because this allows the contribution of O_2 carried in solution (PO_2 x 0.003) to be ignored. If FiO_2 is high (1.0), this will produce a great error during calculation of Q_P/Q_s.

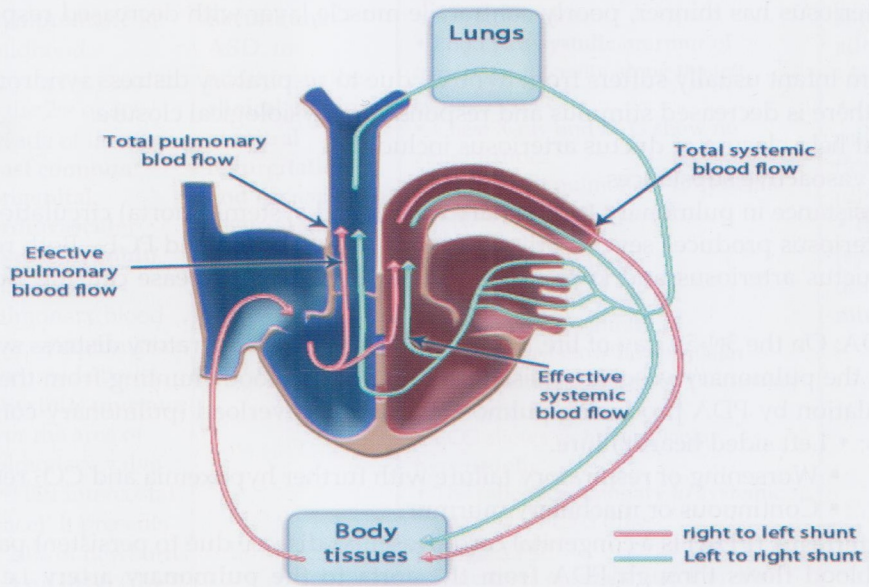


Figure 14-1: Total pulmonary blood flow (Q_P) and total systemic blood flow (Q_s)

The ratio of pulmonary to systemic blood flow depends on:

1. The **size** of the communication.
   - Small sized behaves as **a restrictive shunt.**
   - Large sized behaves as **a non-restrictive shunt.**
2. The relative **balance** between pulmonary and systemic circulation regarding:
   - Pressure gradient.
   - Pulmonary and systemic vascular resistance.
   - Venous return.

These factors are apparent in large sized communications (non-restrictive shunts) i.e., an increase in systemic vascular resistance relative to pulmonary vascular resistance causes an increase in left to right *shunting.*

N.B.: Common chamber lesions e.g., single atrium, single ventricle, or truncus arteriosus represent the extreme forms of non-restrictive shunts; shunt flow with these lesions is bidirectional and totally dependent on relative changes in the ventricular afterload.

Sequences and Complications:

- Increased pulmonary blood flow causes pulmonary vascular congestion which in turn increases extra-vascular lung water. This interferes with gas exchange, decreases lung compliance, and increases the work of breathing.
- Over the course of several years, the **chronic increase in pulmonary blood flow** causes irreversible vascular changes which cause **an irreversible increase in pulmonary vascular resistance**. The latter increases right ventricular afterload and causes right ventricular hypertrophy with a progressive increase in right ventricular pressure. **With advanced disease**, the pressure within the right heart can exceed that within the left heart **resulting in reversal of the shunt** i.e., it becomes right to left **(Eisenmenger's syndrome)**. This occurs in 50% of untreated large VSD and in 10% of untreated large ASD. Reversal of shunt decreases pulmonary blood flow and increases arterial hypoxemia; therefore, cyanosis occurs. It contraindicates surgical correction of congenital heart disease.
- Left atrial distension compresses the left bronchus while pulmonary vascular distension compresses smaller bronchi.

N.B.: Closure of Ductus Arteriosus (DA):

In the fetus, the ductus arteriosus permits pulmonary arterial blood to bypass the deflated lungs and enter the descending aorta for oxygenation in the placenta (i.e., during intrauterine life, the blood flows from the pulmonary artery to the aorta).

Closure of ductus arteriosus occurs in **full term** infant **soon after birth (within 10-15 hours)** due to increased arterial O_2 content (an initial stimulus).

Closure of ductus arteriosus occurs in **preterm** infant after **3-5 days after birth** because:

- Ductus arteriosus has thinner, poorly contractile muscle layer with decreased response to O_2 level after birth.
- The preterm infant usually suffers from hypoxia due to respiratory distress syndrome.

In other words, there is decreased stimulus and response to physiological closure.

Other factors that help closure of ductus arteriosus include:

- Release of vasoactive substances.
- Relative resistance in pulmonary (pulmonary artery) and systemic (aorta) circulation.
- Ductus arteriosus produces several prostaglandins (PGs) as PGI_2 and PGE_2. Both relax the smooth muscle of ductus arteriosus and keep it patent after birth PGs decrease causing closure of ductus arteriosus.

The effects of PDA: On the 3rd-5th day of life, some resolution of the respiratory distress syndrome occurs, which decreases the pulmonary vascular resistance. This allows blood shunting from the systemic to the pulmonary circulation by PDA producing pulmonary vascular overload (pulmonary congestion), which in turn produces:

- Left sided heart failure.
- Worsening of respiratory failure with further hypoxemia and CO_2 retention.
- Continuous or machinery murmur.

Patent ductus arteriosus (PDA) is a congenital cardiovascular disease due to persistent patency of ductus arteriosus. The blood flows through PDA **from the aorta to the pulmonary artery** i.e., a left-to-right shunt.

Persistence of fetal circulation is a condition that occurs after birth due persistence of increased pulmonary vascular resistance e.g., with congenital diaphragmatic hernia where the blood flow continues to flow from the pulmonary artery to the aorta.

Simple Shunts include

	Secundum Atrial Septal Defect (ASD)	Primum Atrial Septal Defect (ASD) (Endocardial Cushion Defect)	Ventricular Septal Defect (VSD)	Patent Ductus Arteriosus (PDA)
Incidence	10% Males > females	3%	28%	10%
Site of defect	• In the center of the interatrial septum (figure 14-2). • Vary from a single opening to a fenestrated septum. • It is usually **isolated**. Sometimes it is associated with mitral valve prolapse.	• A large opening in the interatrial septum. • It is usually associated with **Mitral or tricuspid regurgitation** (or both).	VSD varies from a single opening to a fenestrated septum. It is usually associated with **aortic regurgitation**. Types: • **Type I (5%)**: It is located above the crista supra-ventricularis (a muscular ridge that separates the body of the right ventricle from the pulmonary artery outflow tract) i.e., **supra-cristal defect.** • **Type II (80%)**: It is located in the membranous septum below the crista supra-ventricularis i.e., **infra-cristal defect**. • **Type III (11%)**: It is inlet VSD that accompanies complete AV canal. They result from partial failure of the endocardial cushions to fuse i.e., **canal type**. • **Type IV (4%)**: Due to excessive resorption of septal tissues during the muscular septal formation. They may be located anywhere in the muscular septum and may be multiple (know as **the Swiss Cheese Defect)** i.e., **muscular defect.**	• It connects the aorta (systemic circulation) and pulmonary artery (pulmonary circulation) where the blood flow passes from the aorta to the pulmonary artery. • It arises just **distal to the left subclavian artery**.
Clinical picture In all • It may be asymptomatic if small and can appear at adulthood. • There is clinical picture of **increased pulmonary blood flow.** • There is systolic murmur (except in PDA). • Associated with..... • **Investigations** Chest X-ray. ECG	• If isolated, it is **asymptomatic** in childhood. • Symptoms occur in the 2nd or 3rd decade of life **(the most common congenital cardiovascular disease in adult)**. • Increased pulmonary blood flow symptoms (as discussed above). • **Systolic murmur:** over the area of pulmonary valve (2nd left intercostal space). It presents in 20% of newborns and up to 80% by 5 years of age. There is also a widely	The **same as Secundum ASD**, in addition to the clinical picture of **mitral regurgitation and tricuspid regurgitation.**	**a. Small VSD:** • **Asymptomatic** • Loud **pan-systolic** murmur of maximum intensity along the left sternal border. • Chest X-ray and ECG show no abnormalities. • The ratio of pulmonary to systemic blood flow is < 1.5 by cardiac catheterization. **b. Moderate VSD:** • Asymptomatic • The murmur is louder. • Chest X-ray show biventricular enlargement and increased pulmonary blood flow. • ECG shows right ventricular hypertrophy. • The ratio of pulmonary to systemic blood flow is 1.5-3 times. **c. Large VSD:** • Symptoms occur early in life; often at about 4 weeks of age, as increased pulmonary blood flow symptoms. • The murmur is loudest.	- Most patients are asymptomatic till adolescence. - Symptoms are • Increased pulmonary blood flow symptoms (discussed above) • Continuous (systolic and diastolic) **machinery murmur.**

Echo-cardiography Cardiac catheter-ization	fixed split S_2. • Mitral valve prolapse is present in 30% of cases. • Dysrhythmias such as atrial fibrillation or supraventricular tachycardia and heart block especially right bundle branch block may occur.		• Chest X-ray and ECG show pulmonary hypertension. • The ratio of pulmonary to systemic blood flow is > 3 times. • Later on reverse of the shunt occurs causing cyanosis (Eisenmenger's syndrome) + VSD may be associated with: • Aortic regurgitation. • Gerbode defect: a left ventricular to right atrial septal defect **(Gerbode defect)** that is associated with cardiac conduction disturbances and tricuspid regurgitation.	
Treatment	**Surgical closure** • It is indicated when pulmonary blood flow is at least > 1.5-2 the systemic blood flow. • It is contraindicated when pulmonary vascular resistance is nearly equal to systemic vascular resistance i.e., with severe pulmonary hypertension. • Atrial fibrillation, supraventricular tachycardia, and heart block may occur after successful repair.	**Surgical correction** in the 1st decade of life to prevent development of irreversible pulmonary hypertension by 2 steps: a. Initially: Palliative **banding of pulmonary artery** to decrease the magnitude of the shunt. b. Later on, complete repair with treatment of mitral or tricuspid regurgitation. • Atrial fibrillation, supraventricular tachycardia, and heart block may occur after successful repair.	1. In 25% of cases, it closes **spontaneously**. 2. In 50% of cases, it resolves with **medical treatment.** 3. Palliative **pulmonary artery banding** to increase pulmonary vascular resistance and decrease the shunt. 4. **Complete repair** using cardio-pulmonary bypass is indicated when pulmonary to arterial rate exceeds 0.7. It may be followed by 3rd degree heart block.	1- **Surgical ligation** via a left thoracotomy incision (without cardiopulmonary bypass), usually done after 2 years of age. It may cause intracranial hemorrhage, infections, recurrent laryngeal nerve paralysis if it is performed in premature < 28 weeks of gestation. 2. **Indomethacin or ibuprofen**: It closes PDA especially in premature infants with respiratory distress syndrome because it is a potent nonselective inhibitor of PG forming cyclo-oxygenase; so, PGs synthesis is decreased causing closure of DA. Dose: 0.1-0.2 mg/kg every 4 hours for 24 hours causing closure of PDA.
Anesthetic Management	1- **General principles** of anesthetic management are applied (see above) such as avoiding paradoxical air embolism. 2- **Advocate** events that **increase pulmonary vascular resistance** such as mechanical ventilation, and N_2O and events that **decrease systemic vascular resistance** such as volatile agents or vasodilators. 3- **Avoid** events that **decrease pulmonary vascular resistance** such as high O_2 administration and events that **increase systemic vascular resistance** such as sympathetic stimulation or α-agonists. 4- The increase in pulmonary blood flow may **dilute i.v. drugs,** but causes little effects on the clinical response due to the short pulmonary circulation time. N.B.: Avoid excessive increase of obstruction to the right ventricular outflow such as increased myocardial contractility or hypovolemia as this may cause reversal of the shunt; therefore, volatile anesthetic agents and proper fluid replacement are of choice. 5- When **Eisenmenger's syndrome** occurs, the same anesthetic management of right-to-left shunts (tetralogy of Fallot) is applied. 6- **In VSD:** There is an **increase in the delivery of depressant drugs to the heart** because the coronary blood flow is increased due to the hypertrophied ventricles. Therefore, the increase of the volatile agents to achieve rapid induction may cause excessive myocardial depression before cerebral depression. 7- **In PDA: Postoperative hypertension** may occur after ligation of PDA; therefore, continuous infusion of vasodilator drugs e.g., nitroprusside then usage of long acting anti-hypertensive drugs e.g., hydralazine may be required.			

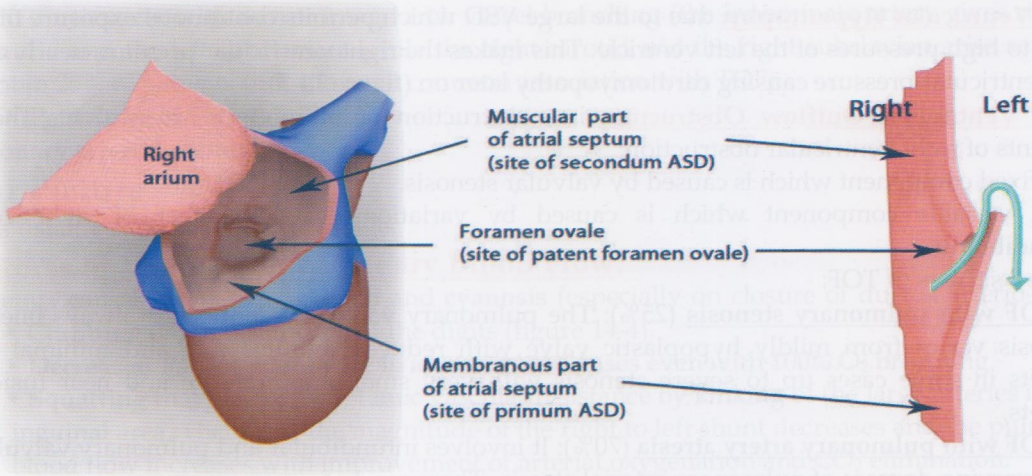


Figure 14-2: The site of primum and secundum ASD

Aorticopulmonary Fenestration

Pathology: there is a communication between the left side of the ascending aorta and the right wall of the main pulmonary artery, just anterior to the origin of the right pulmonary artery. This communication is due to failure of the aorticopulmonary septum to fuse and completely separate the aorta from the pulmonary artery.

Clinical Picture, Investigations, and Anesthetic Management: are similar to those of a large PDA.

Treatment: surgical closure with cardiopulmonary bypass.

Congenital cardiovascular diseases in adult patients:

Adult patients may have one of the following diseases, either treated or not:

- Congenital aortic stenosis.
- ASD (primum or secundum).
- PDA.
- Tetralogy of Fallot.
- Coarctation of the aorta (adult post-ductal type).
- VSD.
- Eisenmenger's syndrome.
- Ebstein's anomaly.

Congenital cardiovascular diseases with adult-onset symptoms include:

- Congenital aortic stenosis.
- ASD (primum or secundum),
- PDA.
- Coarctation of the aorta (adult post-ductal type)
- VSD.

Eisenmenger's syndrome, tetralogy of Fallot, and Ebstein's anomaly are diagnosed early during infancy.

N.B.: Mitral valve prolapse is not a congenital disease but a hereditary or familial disease.

III. Right to Left Intracardiac Shunts

They include: 1. Tetralogy of Fallot.
2. Ebstein's malformation of tricuspid valve.
3. Tricuspid atresia.
4. Patent foramen ovale.
5. Eisenmenger's syndrome.

1. Tetralogy of Fallot (TOF)

It is first described by Fallot in 1888.

Incidence: 10% of all congenital cardiovascular diseases.

Pathology:

TOF consists of:

1- VSD: Typically large, single and sub-aortic.

2- Overriding of the Aorta on the pulmonary artery outflow tract: The shunt has 2 components:

a. A fixed component which is determined by the severity of right ventricular obstruction.

b. A variable component which is determined by systemic and pulmonary vascular resistances.

3- Right Ventricular Hypertrophy: due to the large VSD which permits continuous exposure of the right ventricle to high pressures of the left ventricle. This makes the right ventricular pressure nearly as high as the left ventricular pressure causing cardiomyopathy later on (figure 14-3).

4- Right Ventricular Outflow Obstruction i.e., obstruction of pulmonary artery tract. There are 2 components of right ventricular obstruction:

a. A fixed component which is caused by valvular stenosis.

b. A variable component which is caused by variations in the caliber of right ventricular infundibulum.

There are 3 subsets of TOF:

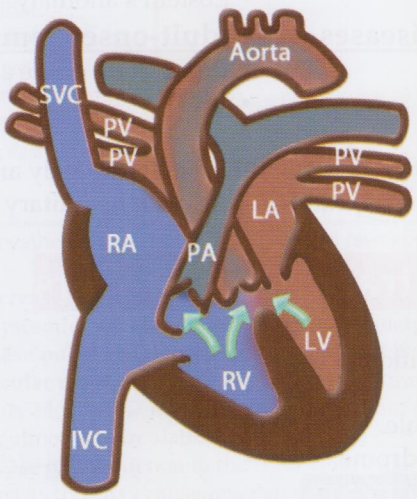
a- TOF with pulmonary stenosis (25%): The pulmonary valve is stenotic and always bileaflet. The stenosis varies from mildly hypoplastic valve with reduced annulus size and minimal fusion of leaflets in some cases up to severe stenosis with very small annulus size and near fusion of the leaflets.

b- TOF with pulmonary artery atresia (70%): It involves infundibular and pulmonary valvular atresia with varying degrees of pulmonary arterial atresia. There are 4 groups:

- **Group I patients:** have isolated infundibular and pulmonary valve atresia with a main pulmonary artery and distal pulmonary arteries of near normal size and architecture. They have pulmonary blood flow supplied from a PDA.
- **Group II patients:** have absence of the main pulmonary artery, but the pulmonary arteries are in continuity and are supplied by a PDA.
- **Group III patients:** have severely hypoplastic native pulmonary arteries; the left and right pulmonary artery may not be in continuity. There are major aortopulmonary collateral arteries (vessels from the aorta to the pulmonary artery) known as MAPCAs. A PDA may be present as well.
- **Group IV patients:** have no native pulmonary arteries and all pulmonary blood flow is derived from MAPCAs.

The pathophysiology of TOF with pulmonary artery atresia can be described as a single ventricle physiology as complete mixing of pulmonary venous and systemic venous blood occurs and the ventricle (s) then distributes output to both the systemic and pulmonary beds.

c- TOF with absent pulmonary valve (rare).



IVC Inferior vena cava
RA Right atrium
RV Right ventricle
PA Pulmonary artery
SVC Superior vena cava
LV Left ventricle
LA Left atrium
PV Pulmonary vein

Figure 14-3: Tetralogy of Fallot

TOF may be associated with:

- **Right aortic arch**: with mirror image arch vessel branching (the innominate artery gives rise to the left carotid and the left subclavian, while the right carotid and the right subclavian arise separately) present in 25% of patients (it is the most common association with TOF).
- **ASD (Pentalogy of Fallot)**.
- **Coronary arterial anomalies**.

Clinical Picture

Symptoms usually start at **6 months of age.**

1. Symptoms of Decreased Pulmonary Blood Flow:

Lung oligemia causes arterial hypoxemia and **cyanosis** (especially on closure of ductus arteriosus) with resulting:

- **Clubbing** of the distal ends of the digits (figure 14-4).
- **Decreased PaO_2 < 50 mm Hg** in arterial blood gases even with 100% O_2 breathing.
- **Squatting** that increases systemic vascular resistance by kinking of the large arteries in the inguinal area. Therefore, the magnitude of the right to left shunt decreases and the pulmonary blood flow increases with improvement of arterial oxygenation and CO_2 elimination.
- **Ejection murmur** heard along the left sternal border due to stenotic pulmonary valve.

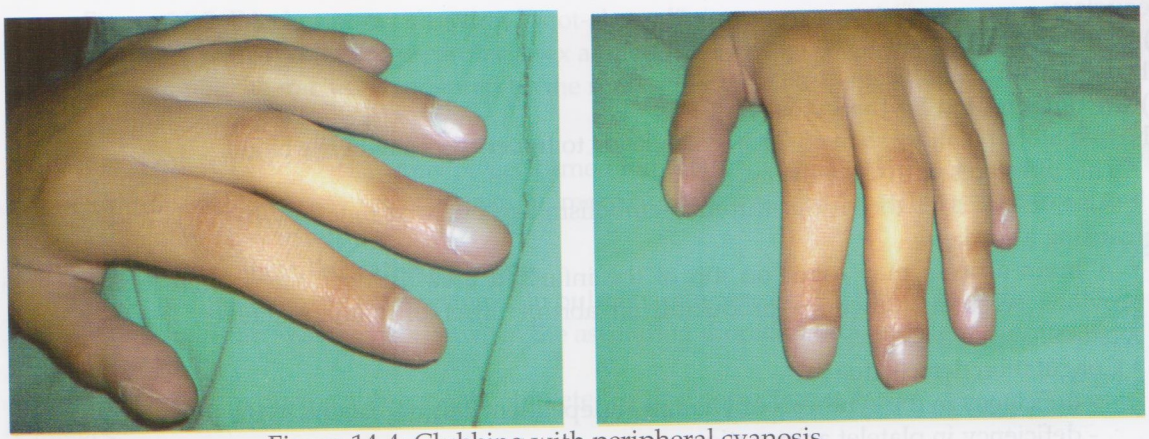


Figure 14-4: Clubbing with peripheral cyanosis

2. Hypercyanotic Attacks (or Tet Spells):

They occur in 35% of patients. The peak incidence is at **the 1st 6 months of age** and decreases with advanced age.

The mechanism is unknown, but a possible cause is sudden decrease in pulmonary blood flow due to:

- spasm of the infundibular cardiac muscle due to sympathetic stimulation by β_2 stimulation.

or

- decreased systemic vascular resistance.

Precipitating factors:

- It can occur spontaneously without obvious provocation.

or

- After effort e.g., crying, exercise, feeding, fever, or defecation.

It is manifested by:

Sudden cyanosis and paroxysmal hyperpnea (hyperventilation) which causes:

- **More arterial hypoxemia** due to increased O_2 consumption through the increased work of breathing.
- **Hypercarbia** due to increased CO_2 production from the contracted muscles.
- **Metabolic acidosis**.

These effects decrease systemic vascular resistance and worsen the shunt.

In some cases, instant loss of consciousness occurs with seizures, as well as cerebrovascular accidents and even death.

Treatment:

1- **Administration of 100% O_2**.

2- **Morphine sulfate** 0.05-0.1 mg/kg to sedate the patient and that may have a central depressant effect on respiratory drive and hyperpnea.

3- **Increase systemic vascular resistance** by one of the following methods:

- **Compression of the femoral arteries** or placing the patient in a **knee-chest position** transiently.

• Manual **compression of the abdominal aorta**. This is performed by the surgeon during opening of the chest **during the surgery** which terminates the cyanotic episode immediately.
• **I.v. fluid administration** of 15-30 mL/kg of a crystalloid solution to:
- increase the heart size which may increase the diameter of the right ventricular outflow tract.
- increase the systemic vascular resistance.
• **Phenylephrine** 5-10 µg/kg i.v. bolus or 2-5 µg/kg/min i.v. infusion.
Avoid *sympathomimetics with* β_2 *agonist effect such as* ***ephedrine*** *as they may cause spasm of the* infundibulum.

4- **Relieve the infundibular spasm:** by β-blockers such as **propranolol** 0.1 mg/kg or **esmolol** 0.5 mg/kg followed by an infusion of 50-300 µg/kg/min. They relieve the spasm by depressing contractility as well as decreasing heart rate that allow for improvement of diastolic filling (increased preload), increase in heart size, and thus increase in diameter of the right ventricular outflow tract.

5- Correction of metabolic acidosis by i.v. **$NaHCO_3$** 1-2 mmol/kg empirically. This helps to neutralize systemic vascular resistance and reduce hyperpnea.

3. 2ry Polycythemia (Erythrocytosis):

Due to chronic hypoxia in cyanotic heart diseases, enhancement of erythropoietin secretion from kidneys occurs to restore tissue oxygen concentration to normal.

Sequelae:

a) Compensated Erythrocytosis:

The hematocrit is stable and **less than 65%**.

b) Uncompensated Erythrocytosis:

The hematocrit is **more than 65-70%** which leads to hyper-viscosity of the blood.

• This interferes with O_2 delivery.
• Also, it increases the risk of thrombo-embolism especially in renal, pulmonary, and cerebral vessels (causing a stroke).
• A brain abscess may occur on top of the infarcted area due to bacterial infection in the areas of previous cerebral infarctions producing an abrupt onset of headache, fever, lethargy, emesis, and seizures.
• Coagulation defects due to:
- deficiency in the synthesis of vitamin K-dependent clotting factors in the liver, and
- deficiency in platelet aggregation.

Precipitating factors of uncompensated erythrocytosis:

• Iron deficiency which makes red blood cells more rigid and less deformable in the microcirculation which increases the viscosity.
• Dehydration.

Treatment of uncompensated erythrocytosis: is mainly phlebotomy and blood replacement with crystalloids.

4. Pink Tet (Acyanotic Tet):

Patients with tetralogy of Fallot have great pulmonary blood flow secondary to the naturally occurring large collateral circulation such as: patent ductus arteriosus,
major aortopulmonary collateral arteries (MAPCAs), and
collateral arteries between bronchial, intercostal and coronary arteries.

These collaterals produce left to right shunt i.e., there is a balance between the left to right and right to left shunt; therefore, no cyanosis occurs until the age of 1-2 years.

5. Infective Endocarditis:

It is very common which necessitates prophylactic antibiotics.

6. Death: occurs as follows:

25% die within the first year.
40% die within 4 years.
70% die within 10 years.
95% die within 40 years.

Investigations:

As discussed before with the following notes:

• Echocardiography with color flow Doppler imaging, magnetic resonant imaging, and cardiac catheterization are diagnostic
• ECG shows right axis deviation and right ventricular hypertrophy.

- Chest X-ray: shows decreased lung vascularity. The heart appears "boot-shaped" with an unturned right ventricular apex and a concave main pulmonary arterial segment (figure 14-5).
- Arterial blood gases show PaO_2 < 50 mm Hg in spite of 100% O_2 administration. $PaCO_2$ and arterial pH are usually normal.

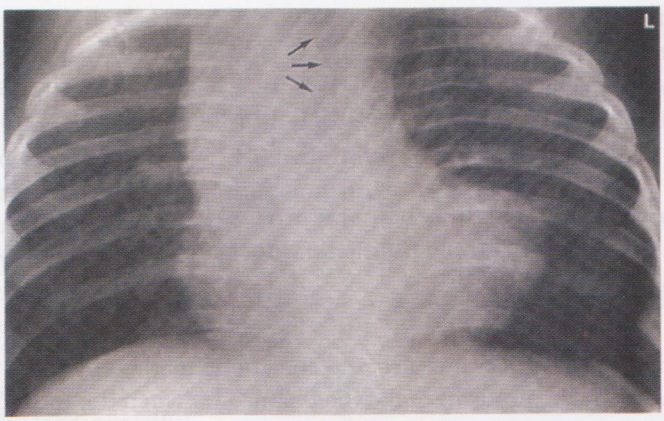


Figure 14-5: PA chest x-ray showing "boot-shaped" appearance of the heart in a patient with TOF with the cardiac apex angled upward, and the lung fields oligemic. The trachea is indented by the right-sided aortic arch (arrowed)

Treatment:

1) Palliative Surgical Procedures may be performed initially:

They increase pulmonary blood flow which causes pulmonary vessel enlargement. It increases PaO_2 and decreases polycythemia. They include:

a- Balloon dilation during cardiac catheterization.

Other surgical procedures are palliative systemic to pulmonary artery shunts which include:

b- Waterston shunt: It is an anastomosis between the ascending thoracic aorta and right pulmonary artery.

Advantages: Its takedown during subsequent complete surgical correction is easier.

Disadvantages:

- Excessive increase in pulmonary blood flow may be produced causing pulmonary hypertension and congestive heart failure.
- Right pulmonary artery thrombosis may occur.

c- Blalock-Taussing shunt: It is an anastomosis between a branch of the ascending thoracic aorta and one of the pulmonary arteries (e.g., end to side anastomosis between the left subclavian artery and the right pulmonary artery on the side opposite to aortic arch).

Advantages: It is associated with lower incidence of the pulmonary hypertension than other types.

Disadvantages:
- Thrombosis of the shunt may occur.
- Subclavian steal syndrome may occur.

d- Potts shunt: It is side-to-side anastomosis of the descending aorta to the left pulmonary artery.

2) Complete Surgical Repair is done later.

It is done at **ages of 2-10 months by cardiopulmonary bypass.** It consists of:

1. Closure of VSD with Dacron patch (without correction of the overriding aorta); therefore, the aorta will be functionally in the left ventricle.
2. Enlargement of the pulmonary artery outflow tract by placement of a synthetic graft or by a pericardial patch.
3. Excision of infundibular bundles of the muscle.
4. Takedown (dismantling) of any previous shunt.

Complications after complete surgical repair:

1. Low cardiac output states may occur due to:
   - Injury of an anomalous anterior descending coronary artery.
   - Persistent VSD.
   - High right ventricular pressure after the repair.
   - Large persistent aorto-pulmonary collaterals.
   - Cardiac tamponade.

2. Residual VSD or right ventricular outflow tract obstruction.
3. Pulmonary regurgitation.
4. Coagulopathy.
5. Heart block and conduction defects.
6. Phrenic nerve injury.
7. Acute renal failure.
8. Patent foramen ovale which causes right to left shunt. This shunt acts as a safety valve if the right ventricle is unable to function with the same efficiency of the left ventricle.
9. Infection.
10. Dysrhythmias.
11. Sudden death due to acute congestive heart failure in 50% of patients,
acute or chronic pulmonary dysfunction in 25% of patients.

Anesthetic Management:

Aim:

Beside the general anesthetic aims and principles, the anesthetic management is nearly opposite to that of the left to right shunt. The primary aim is to make the balance between the pulmonary and arterial blood flow.

1- General Aim and Principles

- Meticulous exclusion of air bubbles or clots from tubing of i.v. fluids is required to avoid paradoxical air embolism into the cerebral or coronary circulation, regardless of the direction of the blood flow.
- Avoid dehydration and follow the preoperative fasting guidelines. **I.v. fluid infusion should be maintained** to avoid any further increase in the blood viscosity.
- Avoid severe myocardial depression. Actually **the increased myocardial contractility** should be also **avoided** because it may increase infundibular obstruction against the right ventricle.
- Maintain sinus rhythm whenever possible.
- Provide sedation and close monitoring.
- Antibiotic prophylaxis against infective endocarditis is essential.

2- Avoid Events that Decrease Systemic Vascular Resistance and Advocate Events that Increase Systemic Vascular Resistance: such as:

- Avoid deep anesthesia and maintain lights anesthesia.
- Avoid α-blockers and advocate α-agonist if needed.
- Physical manipulations (compression of the femoral arteries by flexing the hips of infants and small children i.e., squatting) may be required.
- Avoid hypoxemia, severe hypercarbia, acidosis, and histamine releasing drugs.
- Avoid vasodilator drugs such as volatile anesthetic agents, ganglion blockers, β-agonists, Ca^{++} channel blockers, and phosphodiesterase III inhibitors.

3- Avoid Events that Increase Pulmonary Vascular Resistance and Advocate Events that Decrease Pulmonary Vascular Resistance: such as:

- Administration of high O_2 concentration (FiO_2) and avoiding hypoxia, hypercarbia, acidosis, and histamine releasing drugs.
- Avoid administration of N_2O.
- Avoid high lung volumes or pressures (tend to collapse pulmonary capillaries) such as mechanical ventilation with high airway pressures or positive end expiratory pressure (PEEP). Clinically, mechanical ventilation with airway pressure less than 15 mm Hg can be used safely.

Opening of the chest causes loss of negative intrapleural pressure and increases pulmonary vascular resistance, but actually mechanical ventilation offsets this effect.

- Avoid low lung volumes with atelectasis (tend to collapse pulmonary blood vessels).
- Avoid hypothermia.

Preoperative Management:

Preoperative assessment and diagnosis are discussed above.

1- **Avoid dehydration** by maintaining oral feeding or i.v. fluid preoperatively.

2- **Continue β_2 blockers** until the induction of anesthesia if they have been used as a prophylaxis against hyper-cyanotic attacks.

3- **Avoid i.m. injection** in premedication as it can cause crying that initiates hypercyanotic attack.

4- Severe polycythemic patients should undergo **hemodilution** to hematocrit of 55-60% preoperatively.

5- Allow heavy premedications such as morphine sulfate. Anticholinergics may be needed to decrease the bradycardic effect of induction agents.

Intraoperative Management:

Monitoring:

Besides the standard monitors:

- **Pulse oximetry and invasive blood pressure** should **not be placed on the extremity that is to be involved in the shunt** or that might have been involved in a previous palliative shunt.
- **Central venous catheterization** is done during the complete surgical repair, but the central venous catheter should be **short enough** to avoid the right atrium or superior vena cava cannulas which are inserted by the surgeon as a part of the right heart drainage system.
- **$PaCO_2$ – $PETCO_2$ gradient** is increased > 10-15 mm Hg (it is normally 2-6 mm Hg) due to occurrence of acute reduction of pulmonary blood flow as in decreased cardiac output, pulmonary embolism, or increased right-to-left shunt.
- Arterial line for **invasive blood pressure** and repeated **blood gas sampling**.
- **Urine output**.
- **Temperature probes**.
- **Transesophageal echocardiography.**

Induction:

Preoxygenation is essential.

Induction agent:

- **Ketamine** (i.m. or i.v.) **is of choice** because it increases systemic vascular resistance. It also increases pulmonary vascular resistance, but this is not clinically apparent. Therefore, the net effect is increased pulmonary blood flow with a decrease in the shunt.
- **Other i.v. drugs** will have **a rapid onset** of action because these drugs will reach the systemic circulation rapidly via the right-to-left shunt; therefore, the rate of injection of i.v depressant drugs should be decreased.
- **Inhalational induction is generally avoided but, inhalational induction by sevoflurane** is a good choice in mild shunts because it decreases the myocardial contractility, but care should be taken as it may decrease systemic vascular resistance which may precipitate hypercyanotic attacks; therefore, O_2 monitoring is essential during induction.

Halothane is more preferred because it decreases contractility and relatively maintains systemic vascular resistance.

The inhalational anesthetic agents have **rapid onset** of action due to presence of decreased pulmonary blood flow.

Maintenance:

Ketamine $\pm$ N_2O + Opioids or benzodiazepines + Muscle relaxant + mechanical ventilation.

- **Ketamine** is usually used due to the above advantages.
- **N_2O**: can be used in concentration of **only 50%** because of the following controversial opinions:
  - It increases pulmonary vascular resistance (but this effect is clinically less than the effect of volatile agents on the decreased systemic vascular resistance); so, the net effect is decrease in the shunt if **N_2O is used with volatile agents.**
  - It is associated with a decrease in inspired O_2 concentration. Theoretically the increase in inspired O_2 concentration decreases pulmonary vascular resistance which decreases the shunt; so, improvement of PaO_2 occurs.
  - It has no effect or produces modest increase in systemic vascular resistance which offsets its effect on pulmonary vascular resistance.
- **Opioids or benzodiazepines**: should be used with adjusted doses and rates of administration to decrease their effects on systemic vascular resistance and blood pressure.
- **Muscle relaxants**:

  Pancuronium is of choice because:

  it maintains systemic vascular resistance, and

  it increases the heart rate and maintains left ventricular cardiac output.

  Vecuronium, cis-atracurium, pipecuronium, and doxacurium can be used because they have little effect on the cardiovascular system.

  Atracurium and other muscle relaxants that produce histamine release should be avoided.

- **Mechanical ventilation** should be **used with care** with the following parameters:
  - Rapid rate to induce hypocapnia.
  - The airway pressure should be low as possible < 15 mm Hg.
  - High inspired O_2 concentration.

Intraoperative Fluids Administration:

It should be **maintained** with i.v. crystalloids to avoid acute hypovolemia which increases the shunt. **Blood transfusion** is indicated only when **20%** of blood volume is lost due to the associated polycythemia (in other pediatric cases, blood transfusion is given when 10% of blood is lost). Better to use fresh blood to provide clotting factors.

Cardiopulmonary bypass:

It is required for correction of tetralogy of Fallot. It is discussed in the chapter of "Cardiac Surgery".

Intraoperative Complications:

Hypercyanotic spells may occur intraoperatively due to either hypotension or infundibular spasm. It should be treated as above.

Postoperative Management:

Postoperative complications are according to the type of repair (see before).

Other Right-to-Left Shunts

In addition to tetralogy of Fallot and Eisenmenger's syndrome, there are:

	Ebstein's Malformation of The Tricuspid Valve	Tricuspid Atresia	Patent Foramen Ovale (PFO)
Pathology	It consists of: 1. Downward displacement of the tricuspid valve into the right ventricle causing **obstruction of right ventricular** filling which causes decreased right ventricular size and tricuspid regurgitation. Therefore, **right heart failure** occurs (detected by increased right atrial pressure). 2. The mitral valve may have abnormal placement of leaflets. 3. The **right atrium** is almost always **enlarged**. Massive enlargement of the right atrium causes compression of the apical portions of the lungs resulting in a **restrictive pulmonary disease.** 4. **Right to left shunt** via a **patent foramen ovale** or an associated ASD can be increased during induction of anesthesia. This causes arterial hypoxemia and cardiac tachyarrhythmias Clinical picture: • In mild cases, it is asymptomatic until adulthood and may be discovered accidentally in adults. • In severe cases, fatigue, dyspnea, dysrhythmias, hypoxemia and other clinical pictures similar to TOF take place. • 5-10% of patients have WPW syndrome.	It causes: • **Right to left shunt via ASD.** This leads to shift of the un-oxygenated blood to the left side of the heart resulting in **arterial hypoxemia**. • The increased amount of blood reaching the left ventricle causes **left ventricular enlargement.** • No blood reaches the right ventricle; so, the right ventricle becomes small with marked reduction of pulmonary blood flow. Pulmonary blood flow occurs via bronchial vessels. Treatment: by **Fontan operation** by cardiopulmonary bypass. It involves an anastomosis between the right atrium appendage and right pulmonary artery to provide a direct atrio-pulmonary communication. This operation can be also used for treatment of pulmonary atresia.	• If PFO is associated with **increased right atrial pressure**, right to left shunt is produced which causes **arterial hypoxemia** (figure 14-xxxx). • Closure of FO occurs mechanically (functionally), first by increased left atrial pressure > right atrial pressure, then later on, it is closed permanently (it remains open in 10-30% of normal patients). • Previously closed FO can reopen during anesthesia; so, it is detected post-operatively by: 1. Unexplained arterial hypoxemia. 2. Paradoxical air embolism.

Anesthetic Management

The above congenital anomalies are treated **as tetralogy of Fallot** with the same anesthetic aims and principles. The following notes are important during anesthetic management of **tricuspid atresia**:

- Avoid pressor response to intubation as it causes right ventricular failure.
- Positive inotropic drugs (dopamine) ± vasodilators (nitroprusside) may be used to maintain cardiac output and decrease pulmonary vascular resistance.
- Monitoring:
  - Central venous pressure equals to pulmonary artery pressure in these patients. It is used for:
    - assessment of i.v. fluid volume.
    - detection of sudden impairment of left ventricular function which requires inotropic drugs.
  - Pulmonary artery catheter is techniqually difficult to be inserted due to abnormal anatomy.

- Postoperatively:
  - Right atrial pressure equals to pulmonary artery pressure i.e., elevated around 15 mm Hg, but just after cardiopulmonary bypass and in early postoperative period, right atrial pressure should be maintained between 16-20 mm Hg to facilitate pulmonary blood flow.
  - Pleural effusion, ascites and edema of lower limbs can occur, but usually resolve within a few weeks.

IV. Separation of the Pulmonary and Systemic Circulation

Transposition of Great Arteries (TGA)

Incidence: 5% of all congenital cardiovascular diseases.

Pathology: Due to **failure of the truncus arteriosus to spiral,** the aorta arises from the right ventricle (which is not morphologically designed to function as a high pressure system) and the pulmonary artery arises from the left ventricle. Therefore, the pulmonary and systemic circulation function independently (i.e., parallel to each other). This produces **profound arterial hypoxemia** which causes death unless mixing of blood between the two circulations via PFO, ASD, VSD, PDA or broncho-pulmonary collaterals occurs (Figure 14-6).

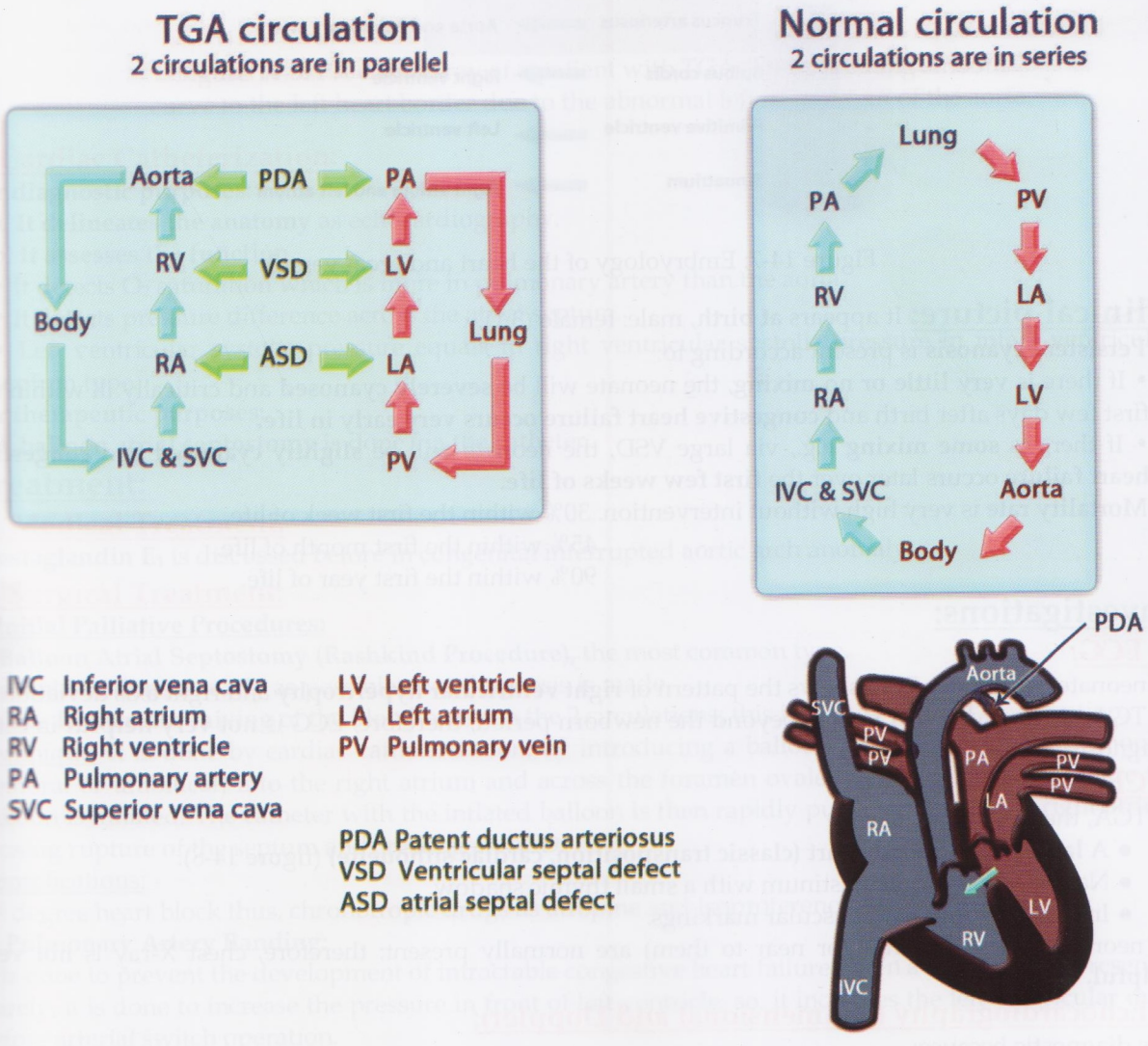


Figure 14-6: TGA (2 circulations are in parallel)

Classification of TGA

Anatomical types	Pulmonary Blood flow	Mixing
1. TGA with intact ventricular septum ± (ASD, PDA or PFO).	↑ (↑)	Little (great)
2. TGA with VSD	↑	Great
3. TGA with VSD and left ventricular outflow tract obstruction	↓	Little
4. TGA with pulmonary vascular occlusive disease. In which, initial increase in pulmonary blood flow causes irreversible medial and intimal hyperplasia of pulmonary vessels which in turn causes pulmonary hypertension. This decreases pulmonary blood flow later resulting in decreased in mixing.	↓ Increased pulmonary blood flow results in increased mixing which in turn decreases the degree of arterial hypoxemia and vice versa.	Little

Types of TGA (according to the anatomical relationship):

In TGA, the aorta lies anteriorly and the pulmonary artery lies posteriorly (normally, the aorta lies posteriorly and to the left while the pulmonary artery lies anteriorly and to the right).

a) D-TGA (dextro-): It is the most common where the aorta lies **anterior** and to the **right** of the pulmonary artery.

b) L-TGA (levo-): where the aorta lies **anterior** and to the **left** of the pulmonary artery.

Embryology of TGA:

The chambers and the great vessels are derived embryologically as shown in figure 14-7.

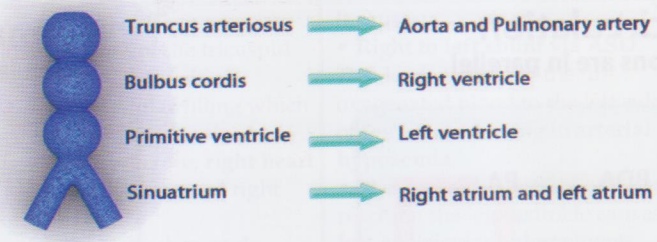


Figure 14-7: Embryology of the heart and great vessels

Clinical picture: It appears **at birth**, male: female (3:1).

1. **Persistent cyanosis** is present according to:
   - If there is **very little or no mixing**, the neonate will be **severely cyanosed** and critically ill within the first few days after birth and **congestive heart failure occurs very early in life.**
   - If there is **some mixing** e.g., via large VSD, the neonate will be **slightly cyanosed** and **congestive heart failure** occurs later over the **first few weeks of life.**
2. **Mortality rate** is very high without intervention. 30% within the first week of life.
   45% within the first month of life.
   90% within the first year of life.

Investigations:

1. ECG:

In neonates, **normally** ECG shows the pattern of **right ventricular hypertrophy** and right axis deviation. In TGA, this pattern **will persist** beyond the newborn period; therefore, ECG is **not very helpful** in early diagnosis of TGA.

2. Chest X-ray:

In TGA, there is a triad of:

- A **large egg –shaped heart (classic transposition, cardiac silhouette)** (figure 14-8).
- Narrow superior mediastinum with a small thymic shadow.
- Increased pulmonary vascular markings.

In neonates, these findings (or near to them) are normally present; therefore, chest X-ray is **not very helpful.**

3. Echocardiography (2 dimensional and Doppler):

It is diagnostic because:

a. It delineates the anatomy.

- The location, size and direction of shunts can be seen.

• **Coronary anatomy** is assessed. It shows great variation with TGA as the coronary arteries may arise from:
- the aortic sinuses (sinus of Valsalva) that face the pulmonary artery i.e., posterior portion of the aorta (in normal heart, they arise from aortic sinuses located on the anterior portion of the aorta).
- Single coronary artery (right or left).

Or - Circumflex artery may arise form right (instead of left) coronary artery.

This is important in arterial switch operations.

b. It assesses the function.

• Estimates the ventricular pressures and function.

• In TGA, the pulmonary valve opens earlier and closes later than the aortic valve (the reverse occurs in normal heart).

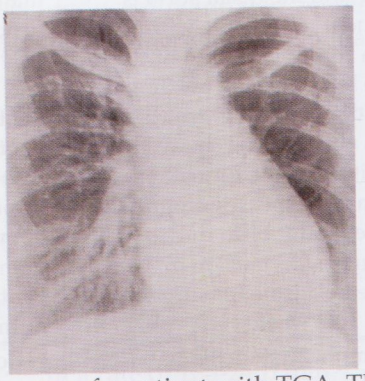


Figure 14-8: PA chest x-ray of a patient with TGA. There is a long smooth curve to the left heart border due to the abnormal leftward origin of the aorta.

4. Cardiac Catheterization:

For diagnostic purposes:

a. It delineates the anatomy as echocardiography.

b. It assesses the function.

• It detects O_2 saturation which is more in pulmonary artery than the aorta.

• It detects pressure difference across the atrial septum.

• Left ventricular systolic pressure equals to right ventricular systolic pressure in intact ventricular septum type.

For therapeutic purposes:

A balloon atrial septostomy is done via the catheter.

Treatment:

A. Medical Treatment:

Prostaglandin E_1 is discussed before in congenital interrupted aortic arch anomaly.

B. Surgical Treatment:

I. Initial Palliative Procedures:

a. Balloon Atrial Septostomy (Rashkind Procedure), the most common type.

It should be done **as early as** possible once diagnosis is made.

Value: To **increase mixing** of the blood between the 2 circulations; this improves arterial oxygenation.

Technique: It is done by cardiac catheterization, by introducing a balloon-tipped catheter intravenously (femoral or umbilical) into the right atrium and across the foramen ovale into the left atrium where the balloon is inflated. The catheter with the inflated balloon is then rapidly pulled back into the right atrium causing rupture of the septum and creating an ASD.

Complications:

3rd degree heart block thus, chronotropic drugs as atropine and isoproterenol should be available.

b. Pulmonary Artery Banding:

It is done to prevent the development of intractable congestive heart failure when a large VSD is present.

Rarely, it is done to increase the pressure in front of left ventricle; so, it increases the left ventricular mass before arterial switch operation.

II. Complete Surgical Correction:

It is performed at **6-9 months** of age. Recently, it can be done in the neonatal period (1st 2 weeks).

It needs cardiopulmonary bypass.

Types:

	1- Arterial Switch Operation (ASO)	Atrial Switch Operation	
		2- Mustard Operation	3- Senning Operation
	It is the most definitive surgical correction done now (of choice) By Jatene in 1975.	It was done in the past	It was done in the past
Technique	• **Surgical translocation and re-anastomosis** of the aorta and the main pulmonary artery (i.e., the great arteries are switched as the distal pulmonary artery is brought anteriorly and anastomosis with right ventricle outflow and the distal aorta is brought posteriorly and anastomoses with left ventricle outflow with **re-implantation of the coronary artery to the left ventricle outflow.** • The success of ASO depends on the **mass of the left ventricle** which is now serving the systemic circulation. In TGA with intact ventricular mass type, left ventricular mass decreases progressively within the first 2-3 weeks after birth due to regression of pulmonary hypertension in neonates soon after birth; so, the **best time** for surgery in these patients is in **the 1st 2 weeks.**	• The atrial septum is removed and replaced with an intra-atrial baffle (tunnel) made of **the pericardium** or **synthetic material** to redirect pulmonary venous blood via the tricuspid valve into the right ventricle and out the aorta (i.e., **the right ventricle remains the systemic ventricle**). Systemic venous blood flows via the baffle through mitral valve into the left ventricle and out of the pulmonary artery (i.e., **the left ventricle remains the pulmonic ventricle**).	• The same as Mustard operation, but the baffle is made of **autologous right atrial tissue and inter-atrial septum** instead of pericardium or synthetic materials.
Complications	1. **Supra-valvular pulmonary stenosis.** 2. **Aortic regurgitation.** 3. **Dysrhythmias** as premature atrial and ventricular contractions. 4. **Myocardial ischemia** related to re-implantation of coronary arteries. Therefore, coronary anatomy should be known before surgery. 5. **Left ventricular dysfunction** due to inadequate left ventricular mass. 6. **Sinus node artery damage:** It is usually the first branch of the right coronary artery close to its origin). It increases the risk of atrial arrhythmias and heart block.	1. **Conduction defects and arrhythmias** due to surgical manipulation of conductive tissues. 2. **Pulmonary venous congestion** due to baffle construction. 3. **Tricuspid regurgitation.** 4. **Right ventricular dysfunction** because the right ventricle is not morphologically designed to function as the systemic ventricle. 5. Since the Senning repair involves the use of in situ tissues, it is less restrictive over time than Mustard repair.	

4. Rastelli Operation:

It is done in TGA with left ventricular outflow obstruction.

Technique: VSD is closed. Pulmonary outflow tract is done by a Dacron conduit that contains an artificial valve. It restores the normal pumping function of ventricles (i.e., the left ventricle is systemic and right ventricle is pulmonic).

5. Fontan Operation:

It can be done, as in tricuspid atresia.

Anesthetic Management:

Aim:

The primary aim is to make a balance between the systemic and pulmonary blood flow through adjusting the systemic and pulmonary vascular resistance.

The anesthetic aims and principles are nearly **the same as tetralogy of Fallot**.

1- General aims and principles.

2- Avoid Events that Decrease Systemic Vascular Resistance and Advocate Events that Increase Systemic Vascular Resistance:

3- Avoid Events that Increase Pulmonary Vascular Resistance and Advocate Events that Decrease Pulmonary Vascular Resistance:

They are discussed in details in tetralogy of Fallot.

Preoperative Management:

Preoperative assessment and diagnosis is discussed above.

1- **Avoid dehydration** by maintaining oral feeding or i.v. fluid infusion preoperatively.

2- Severely cyanotic infants may require **PGE_1.**
3- **Correction of metabolic acidosis**.
4- Premedications: because patients are usually infants, there is no need for premedications.

Intraoperative Management:

Monitoring, induction, and maintenance are the same as tetralogy of Fallot with the following notes:

- N_2O is better avoided because of the need for high inspired O_2 concentration.
- Volatile agents should be avoided.
- Due to separation of the pulmonary and systemic circulation by TGA:
  - **I.v. drugs** will be distributed with minimal dilution to organs e.g., the heart and brain; so, **doses and rates** of i.v. drugs should be **reduced.**
  - Conversely, the **onset** of anesthesia produced by **inhaled** agents (if used) will be **delayed**, as only small amounts of the inhaled drug will reach the systemic circulation.

Postoperative Management:

1- **Controlled ventilation** is needed in infants in the immediate postoperative period till the patient is hemodynamically stable.
2- **Postoperative complications** are according to the type of repair (see above).

N.B.: Junctional Ectopic Tachycardia (JET):

It is a rare tachycardia that occurs in the early postoperative period in infants with congenital heart diseases treated with cardiopulmonary bypass.

ECG: • Tachycardia; transient usually turns to sinus rhythm within 24-72 hours.
• QRS complex is of normal shape with a rate of 180-240/min.
• With atrioventricular dissociation.

Cause: is unknown, but may be due to enhanced automaticity of tissues in or near the AV node as a result of surgical trauma.

Complications: It causes hemodynamic instability.

Treatment:

1- Procainamide and propafenone are effective, but due to their negative inotropic effects they may not be used if there is hemodynamic instability.
2- Induced hypothermia (up to 31-34°C) decreases the heart rate to be < 180/min, but it may produce peripheral vasoconstriction, metabolic acidosis, and agitation.

V. Mixing of the Pulmonary and Systemic Circulation

As a result of this mixing, symptoms are according to the ratio of pulmonary to systemic blood mixing i.e., the amount of pulmonary blood flow.

- Increased pulmonary blood flow leads to pulmonary congestion and congestive heart failure. Cyanosis is not severe or does not occur (O_2 saturation in the pulmonary blood is higher than systemic blood).
- Decreased pulmonary blood flow leads to pulmonary oligemia and severe cyanosis.

They include:

	Hypoplastic Left Heart Syndrome	Truncus Arteriosus	Partial Anomalous Pulmonary Venous Return	Total Anomalous Pulmonary Venous Return	Double Outlet Right Ventricle
Pathology	• There is **left ventricular hypoplasia**, mitral valve hypoplasia, aortic valve atresia, and ascending aorta hypoplasia. • There is mixing of the pulmonary venous and systemic venous blood in a single ventricle (right) which is connected to systemic arteries by PDA. • Just after birth, abrupt fall in pulmonary vascular resistance occurs which increases the pulmonary blood flow (and decreases the systemic blood flow).	**There is a single arterial trunk** which gives the aorta and pulmonary artery. This single arterial trunk overrides both ventricles which are connected via VSD.	**Either left or right pulmonary vein drain into the right side of the circulation (rather than the left atrium).** They drain either: • 50% in superior vena cave, • 50% in right atrium, inferior vena cava, azygos vein or coronary sinus. Therefore, mixing of pulmonary and	**The 4 pulmonary veins drain into the right side of the heart** (rather than left side). The oxygenated blood will reach the left atrium by ASD ± PDA. This increases pulmonary blood flow very	**The aorta arises from the posterior wall of the right ventricle.** The left ventricle outflow occurs through VSD allowing

	i.e., **pulmonary steal phenomenon.** This causes high cardiac output failure, metabolic acidosis and ventricular failure (although there is increased PaO_2). Any factor that increases pulmonary vascular resistance leads to a decrease in the pulmonary blood flow with hypoxia which in turn causes metabolic acidosis and collapse.	Therefore, mixing of pulmonary and systemic circulation occurs producing symptoms according to the degree of the pulmonary blood flow.	systemic circulation occurs producing symptoms according to the degree of the pulmonary blood flow. There is usually slight increase in the pulmonary blood flow causing congestive heart failure at early adulthood.	much causing congestive heart failure in 50% of cases within the 1st month and in the other 50% of cases within the 1st year of life.	blood to reach the right ventricle. This increases the pulmonary blood flow producing congestive heart failure.

Treatment: Surgical correction with cardiopulmonary bypass is required.

In hypoplastic left heart syndrome: PGE_1 can be given to prevent closure of PDA.

Anesthetic Management:

According to the amount of pulmonary blood flow, try to make a balance between the pulmonary and systemic blood flow.

- If the patient is hypoxic (by arterial blood gases), the pulmonary blood flow should be increased by decreasing pulmonary vascular resistance.
- If the patient is hyperoxic and with congestive heart failure, the pulmonary blood flow should be decreased by increasing pulmonary vascular resistance.

N.B.: - In hypoplastic left heart syndrome, ventricular fibrillation is very common to occur.
- In total anomalous pulmonary venous return, i.v. fluid infusions may be dangerous because they are directly delivered to the right atrium then to the lung increasing the risk of pulmonary edema.

VI. Mechanical Obstruction of the Trachea

It is obstruction of the trachea and/or the main bronchus due to circulatory anomalies. It causes unexplained stridor and wheezes and then severe hypoxia occurs.

Esophageal compression may be also present causing dysphagia.

They include

	Double Aortic Arch	Aberrant left pulmonary artery	Absent Pulmonary Valve
Pathology	Double aortic arch acts as a vascular ring which produces pressure on: • **The trachea** causing inspiratory stridor especially with the neck flexed, wheezes, and hypoxia. • **The esophagus** causing dysphagia.	Aberrant left pulmonary artery arises from right pulmonary artery (left pulmonary artery is absent). It passes between the trachea and esophagus causing a vascular sling (not ring). It produces pressure on the **trachea or right bronchus.**	Absent pulmonary valve causes dilation of the pulmonary artery. It produces pressure on the **trachea or left bronchus** (usually with tetralogy of Fallot).
Surgical correction	By removal of the smaller aortic arch.	By division of the artery and placing it anterior to the trachea then re-anastomosing it to the main pulmonary artery.	By insertion of a tubular graft with an artificial pulmonic valve.

Tracheal intubation should be beyond the level of obstruction.

Further Readings:

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CENTRAL NERVOUS DISEASES

15

• Anatomy of the central nervous system Blood supply of the brain • Physiology of central nervous system Cerebral metabolism Cerebral blood flow Blood brain barrier Cerebro-spinal fluid Intracranial pressure • Intracranial hypertension • Brain protection • Anesthesia for craniotomy • Anesthesia for intracranial aneurysm • Subarachnoid Hemorrhage • Anesthetic management of coil placement and interventional neuro-radiology	• Anesthetic management of arterio-venous malformation • Moyamoya disease • Anesthesia for head injury (head trauma) • Anesthetic management of patients with head injury undergoing non-neurologic procedures • Anesthesia for stereotactic surgery and neuro-navigation • Anesthesia for shunt insertion and revision • Anesthesia for spinal surgery Cervical spine • Anesthesia for neurosurgery in infants and children • Complications in neuro-anesthesia

Anatomy of the Central Nervous System

Central nervous system consists of the **brain** and the **spinal cord**.

The brain consists of:

a- **The cerebrum** that consists of:

1- **Diencephalon;** consists in turn of:

- **The thalamus;** contains the nuclei of the main sensory pathways.
- **The hypothalamus;** coordinates the autonomic nervous system and the endocrine system.

The pituitary gland lies below the hypothalamus.

2- **The parietal cerebral hemispheres;** consist in turn of:

- **The cerebral cortex;** is formed of:
  - **Frontal lobe;** contains the motor area and areas of the intellect and behavior.
  - **Temporal lobe**.
  - **Parietal lobe;** is concerned with auditory sensation and integration of the other stimuli.
  - **Occipital lobe;** contains the visual cortex.

A central sulcus or cleft separates the main motor gyrus (or fold) anteriorly from the main sensory gyrus posteriorly.

- **The basal ganglia and internal capsule**.
- **The lateral ventricle.**

b- **The cerebellum** that coordinates balance, posture, and muscular tone.

c- **The brainstem that** consists of:

1- **The midbrain;** connects the brainstem and cerebellum to the hypothalamus.

2- **The pons;** contains many centers of the cranial nerves.

3- **The medulla;** contains the ascending and descending nerve tracts, the lower cranial nerves nuclei and the respiratory and vasomotor centers (i.e., vital centers).

Reticular activating system runs through the brainstem and is responsible for consciousness.

The spinal cord passes from the foramen magnum, where it is continuous with the medulla, to a tapered end termed the conus medullaris at the level of first or second lumbar vertebrae. The spinal cord is formed from 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 5 coccygeal segments (figure 15-1, 15-2, and 15-3).

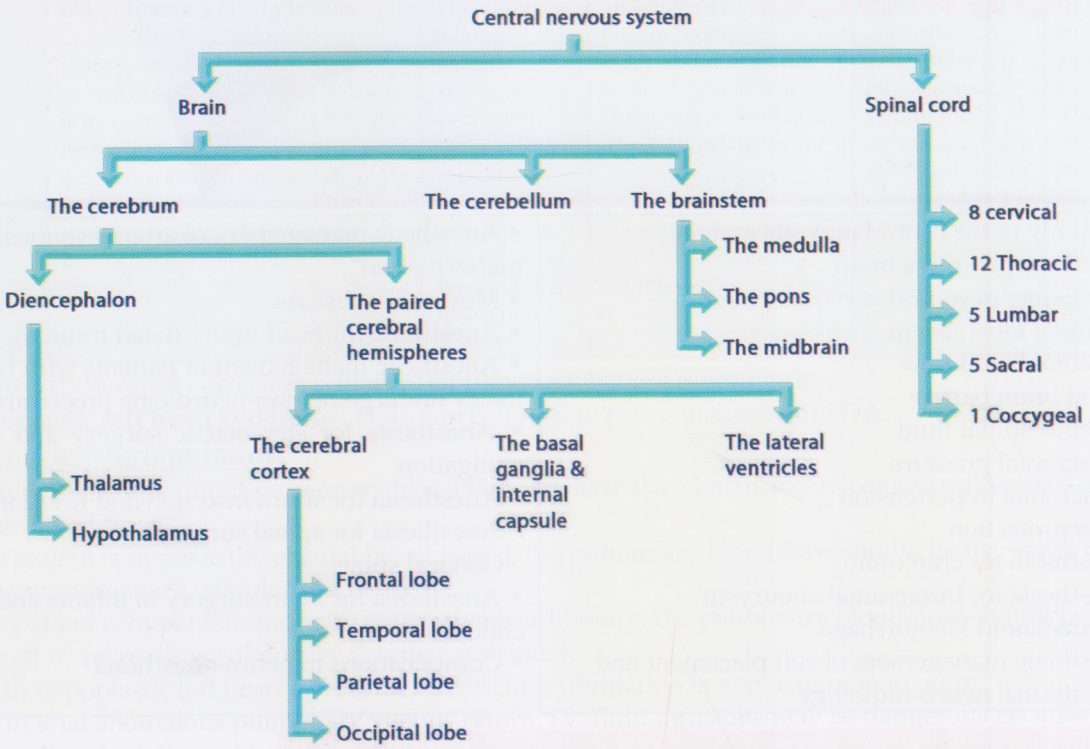


Figure 15-1: Parts of the central nervous system

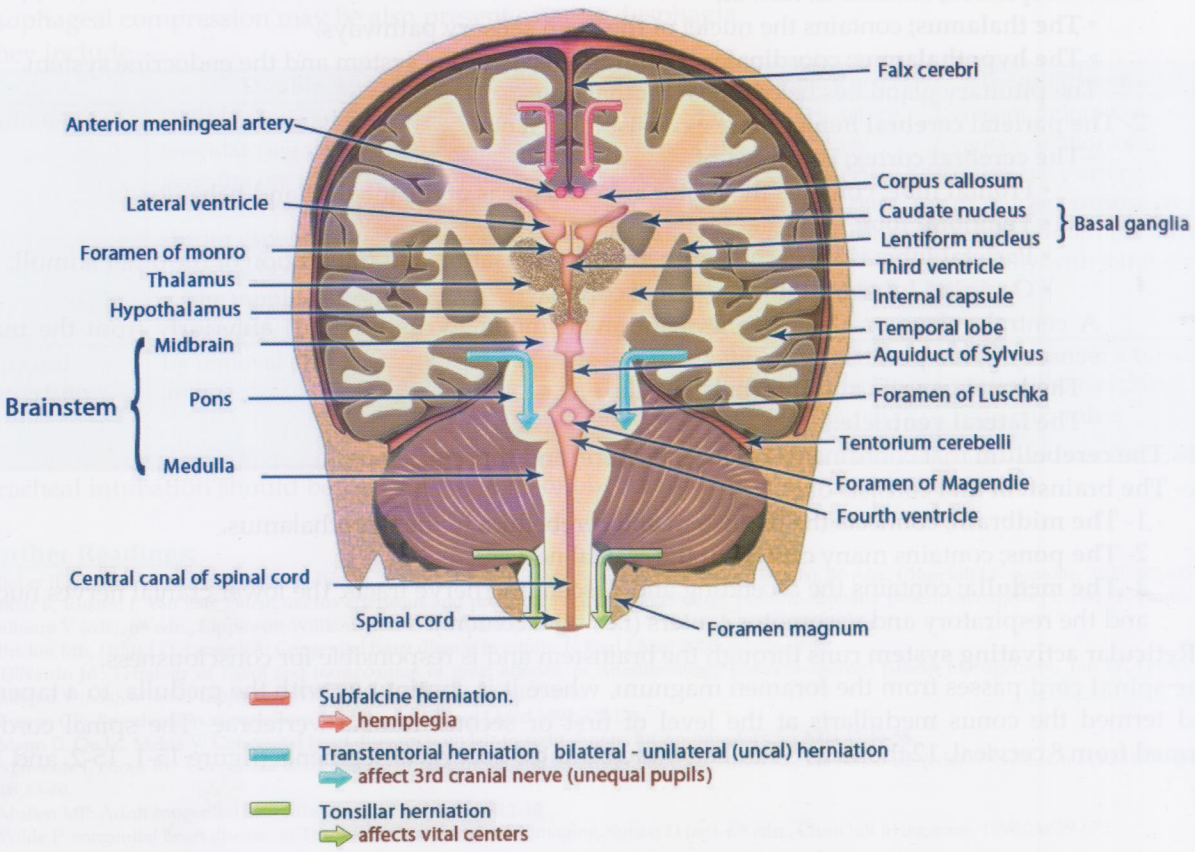


Figure 15-2: Coronal section of the central nervous system

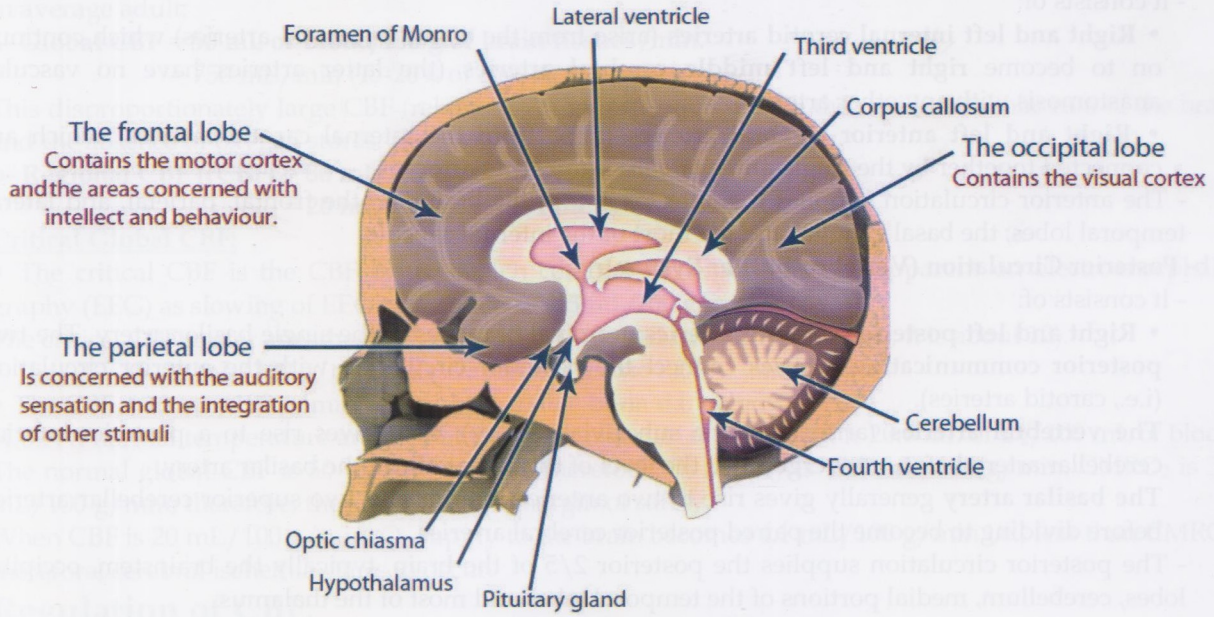


Figure 15-3: Sagittal sections of the central nervous system

Blood Supply of the Brain

Blood supply to the brain is provided by **Circle of Willis.**

Site: It lies in the inter-peduncular fossa at the base of the brain (i.e., the inferior surface) and around the region of hypothalamus.

Formation: It is formed from 6 large arteries (3 on each side) forming anterior and posterior circulations and connected by 3 small communicating arteries (one anterior and two posterior) (figure 15-4).

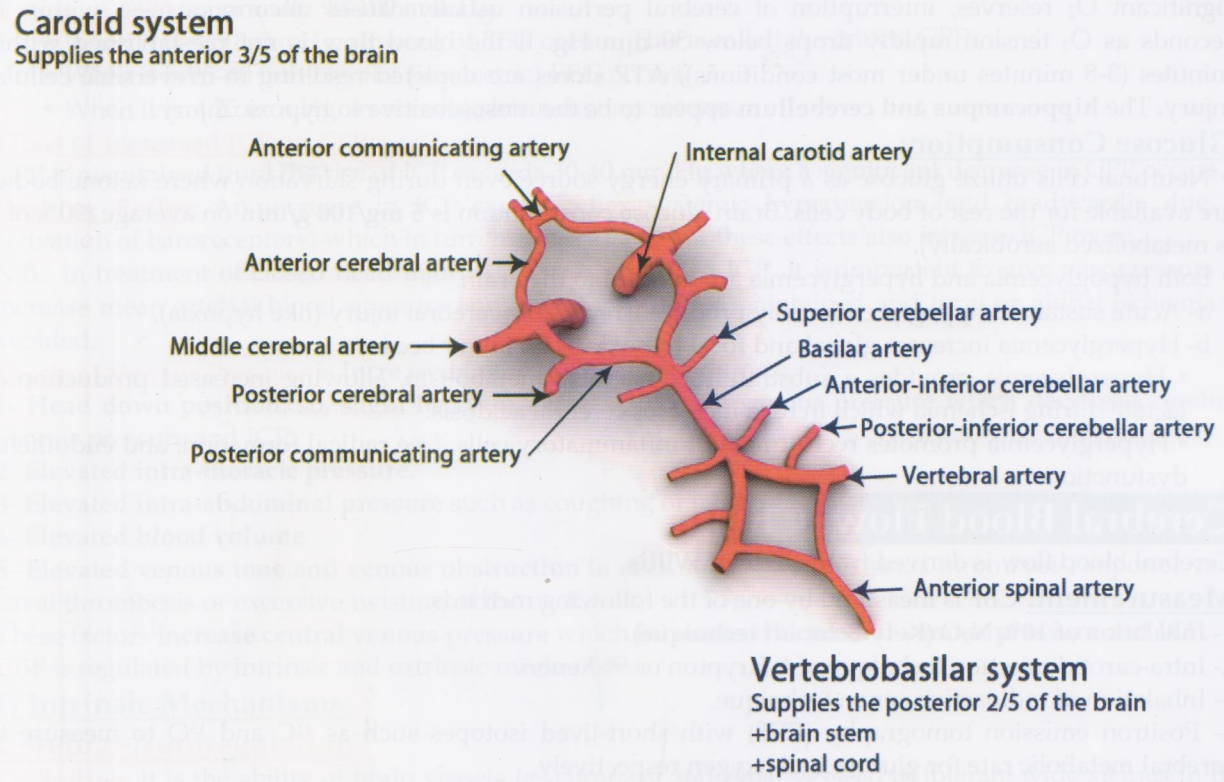


Figure 15-4: Circle of Willis

a- **Anterior Circulation (Carotid System):**

- It consists of:
  - **Right and left internal carotid arteries** (arise from the common carotid arteries) which continue on to become **right and left middle cerebral arteries** (the latter arteries have no vascular anastomosis with any other arteries).
  - **Right and left anterior cerebral arteries** (arise from the internal carotid arteries) which are connected together by the single **anterior communicating artery**.
- The anterior circulation supplies the anterior 3/5 of the brain i.e., the frontal, parietal, and lateral temporal lobes; the basal ganglia, and the most of the internal capsule.

b- **Posterior Circulation (Vertebro-Basilar System):**

- It consists of:
  - **Right and left posterior cerebral arteries**; terminal branches of the single basilar artery. The **two posterior communicating arteries** connect the posterior circulation with the anterior circulation (i.e., carotid arteries).

  The vertebral arteries (arise from the subclavian artery); each gives rise to a posterior-inferior cerebellar artery before convergence at the level of the pons to form the basilar artery.

  The basilar artery generally gives rise to two anterior-inferior and two superior cerebellar arteries before dividing to become the paired posterior cerebral arteries.
- The posterior circulation supplies the posterior 2/5 of the brain, typically the brainstem, occipital lobes, cerebellum, medial portions of the temporal lobes and most of the thalamus.

Physiology of Central Nervous System

Cerebral Metabolism

O_2 Consumption:

- The cerebral metabolic rate (CMR) is usually expressed in terms of O_2 consumption ($CMRO_2$) with an average of **3-3.5 (up to 5) mL/100 g/min (50 mL/min)** in adults. It is calculated by the **Fick's principle**

$CMRO_2$ = Cerebral blood flow x arterial-venous O_2 content difference

$CMRO_2$ does not indicate the nature or extent of cerebral hypoxia.

- Because of the relatively high O_2 consumption (20% of total body O_2 consumption) and the absence of significant O_2 reserves, interruption of cerebral perfusion usually causes unconsciousness within 10 seconds as O_2 tension rapidly drops below 30 mm Hg. If the blood flow is not reestablished within minutes (3-8 minutes under most conditions), ATP stores are depleted resulting in irreversible cellular injury. The **hippocampus and cerebellum** appear to be the most sensitive to hypoxic injury.

Glucose Consumption:

- Neuronal cells utilize glucose as a primary energy source even during starvation where ketone bodies are available for the rest of body cells. Brain glucose consumption is **5 mg/100 g/min** on average (90% of it is metabolized aerobically).
- Both hypoglycemia and hyperglycemia are harmful to the brain.
  - a- Acute sustained hypoglycemia: may produce irreversible cerebral injury (like hypoxia).
  - b- Hyperglycemia increases global and focal hypoxic brain injury because:
    - Hyperglycemia provides a substrate for anaerobic metabolism, allowing increased production of lactate during ischemia which in turn increases cerebral acidosis.
    - Hyperglycemia promotes recruitment of inflammatory cells, free radical formation, and endothelial dysfunction.

Cerebral Blood Flow (CBF)

Cerebral blood flow is derived from **circle of Willis**.

Measurement: CBF is measured by one of the following methods.

1- Inhalation of 10% N_2O (Kety-Schmidt technique).

2- Intra-carotid injection technique of ^{85}Krypton or ^{133}Xenon.

3- Inhalation of radioactive xenon technique.

4- Positron emission tomography (PET) with short-lived isotopes such as ^{11}C and ^{15}O to measure the cerebral metabolic rate for glucose and oxygen respectively.

5- Trans-cranial Doppler.

They are discussed in details in chapter "Monitoring".

Values:

In average adult:

a- Global CBF = 50 mL of blood/100 g of brain tissues /min.

= 750 mL/min (15-20% of cardiac output).

This disproportionately large CBF (relative to other organs) is due to the rapid metabolic rate of the brain and the absence of oxygen stores.

b- Regional CBF (rCBF) = 80 mL/100 g/min for the gray mater.

= 20 mL/100 g/min for the white mater.

Critical Global CBF:

- The critical CBF is the CBF below which cerebral ischemia becomes apparent on electroencephalography (EEG) as slowing of EEG waves. It is **20-25 mL/100 g/min.**

The critical CBF **under anesthesia** is about **18 mL/100 g/min** (with isoflurane, it is about 12).

- The CBF 15- 20 mL/100 g/min causes a flat isoelectric EEG.
- The CBF < 10 mL/100 g/min causes irreversible brain damage.

N.B.: At normal temperature and hematocrit, normal arterial O_2 content is 20.6 mL of O_2/100 mL of blood. The normal global CBF is 50 mL/100 g/min; therefore, O_2 supply is 10.3 mL/100 g/min. $CMRO_2$ is 3-5 mL/100 g/min; therefore, there is a relative margin of safety.

When CBF is 20 mL/100 g/min, O_2 supply to the brain becomes 4.1 mL/100 g/min i.e., less than $CMRO_2$; therefore, cerebral ischemia starts to occur.

Regulation of CBF:

Perfusion pressure is the pressure responsible for driving the blood to an organ.

Perfusion pressure = forcing pressure- opposing pressure

Cerebral Perfusion Pressure (CPP)

= Mean Arterial Pressure (MAP) – Intracranial Pressure (ICP) + cerebral venous pressure

Cerebral (or central) venous pressure is usually not included in the equation because:

- It usually equals zero at the jugular venous bulb.
- ICP is easier to be measured.

Cerebral (or central) venous pressure is included in the equation when it is greater than ICP.

Values of CPP: is normally **90-100 mm Hg.**

- When it is < 50 mm Hg, slowing of EEG occurs. This is called the critical CPP.
- When it is 25-40 mm Hg, flat (isoelectric) EEG occurs.
- When it is < 25 mm Hg, irreversible brain damage occurs.

Effect of increased ICP on CPP:

CPP is maintained until the rise of ICP exceeds 30-40 mm Hg where a significant decrease in CPP occurs.

Cushing Reflex: An increase in ICP causes reflex systemic hypertension (and bradycardia due to activation of baroreceptors) which in turn increases CPP, but these effects also increase ICP more.

N.B.: In treatment of closed head injuries, there is increased ICP. It is important to give vasopressors to increase mean arterial blood pressure and; therefore, CPP is maintained and focal or global ischemia is avoided.

Cerebral Venous Pressure is **increased** in the following conditions:

1- Head down position; so, slight head-up decreases central venous pressure which **decreases** cerebral venous pressure and ICP.

2- Elevated intra-thoracic pressure.

3- Elevated intra-abdominal pressure such as coughing or straining.

4- Elevated blood volume

5- Elevated venous tone and venous obstruction in neck such as venous sinus thrombosis, superior vena caval thrombosis or excessive twisting of the neck.

These factors **increase central venous pressure** which **increases** the **cerebral venous pressure** and **ICP**.

CBF is regulated by intrinsic and extrinsic mechanisms.

I) Intrinsic Mechanisms:

Cerebral Autoregulation

Definition: It is the ability of brain vessels (as coronary and renal vessels) to tolerate wide swings in the mean blood pressure **(between 50-150 mm Hg)** with little changes in the CBF.

A decrease in CBF decreases CPP; this causes cerebral vasodilation and increases CBF again to reach its previous level and an increase in CBF increases CPP; this causes cerebral vasoconstriction and decreases CBF again to reach its previous level.

Beyond these limits (i.e., < 50 and > 150 mm Hg), **CBF becomes pressure dependant** i.e., CBF changes with the change of blood pressure.

- **Above 150 mm Hg**, the cerebral blood vessels are maximally constricted, but CBF increases because it is pressure dependent. This results in over-distention of the brain tissues, producing **cerebral edema**.
- **Below 50 mm Hg**, the cerebral blood vessels are maximally dilated, but CBF decreases because it is pressure dependent. This results in **cerebral ischemia**.

Cerebral Autoregulation Curve (and Causes of Impaired Autoregulation)

a- **It is shifted to the right** (both upper and lower limits) in the following conditions:

- Hemorrhagic hypotension as it is associated with excessive sympathetic activity.
- Chronic arterial hypertension.

Both conditions are characterized by vasoconstriction of blood vessels.

This means that:

- Hypertensive patients can tolerate marked increases in MAP much better than normotensive patients. Acute hypertension as seen in children with acute onset glomerulonephritis, females with short-duration pregnancy-induced hypertension, or patients during direct laryngoscopy or under stress of surgery often produces signs of central nervous dysfunction at mean arterial pressure (MAP) elevations tolerated by patients who are chronically hypertensive.
- The reverse occurs at low MAP of 60 mm Hg or less, which would be tolerated in normotensive patients, but it may actually be below the lower limit of autoregulation in hypertensive patients causing cerebral hypoperfusion.

N.B.: Chronic antihypertensive treatment may restore cerebral autoregulation limits to normal.

b- **It is shifted to the left** (both upper and lower limits) in vasodilator-induced hypotension. Na nitroprusside causes more shift to the left than trimethaphan (figure 15-5).

c- Autoregulation is abolished (i.e., absence of the plateau of the curve) in the following cases:

- Hypoxia and hypercapnia.
- Premature infants.
- Acute increase in ICP as in head trauma or intracerebral tumors.
- Use of potent volatile anesthetics (except N_2O).
- Inhibition of nitric oxide (NO) synthesis which abolishes the cerebral autoregulation i.e., intrinsic mechanism, and abolishes cerebral vasodilation in response to hypercapnia, hypoxia and volatile anesthetics i.e., external mechanisms (see later).

In these conditions, the cerebral blood vessels lose their vasodilator and vasoconstrictor mechanisms.

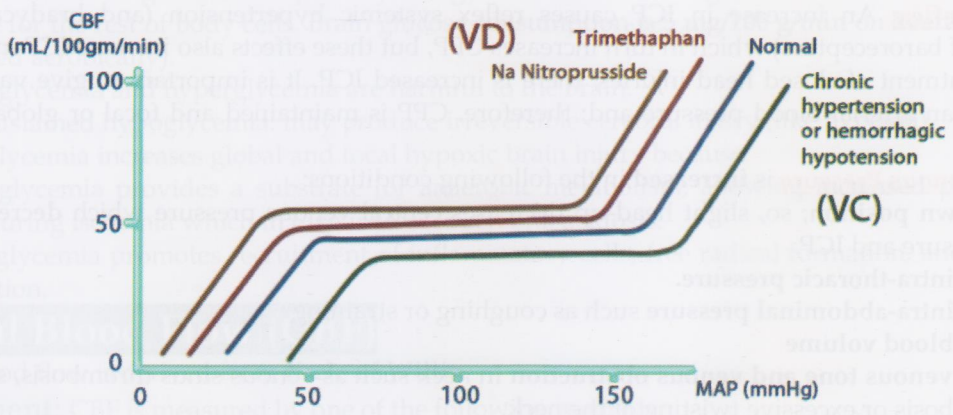


Figure 15-5: Cerebral Autoregulation Curve; VD is vasodilation and VC is vasoconstriction.

Mechanisms of autoregulation: There are two theories:

1- Myogenic Theory:

It is the intrinsic response of smooth muscle cells in cerebral arterioles to the changes in mean blood pressure i.e., an increase in the mean blood pressure causes distension of arteriolar wall that in turn

causes contraction of arteriolar vascular smooth muscle. This decreases arteriolar diameter and decreases CBF.

2- Metabolic Theory:

Release of tissue metabolites such as nitric oxide, adenosine, prostaglandins and electrolytes causes vasodilation which leads to an increase in CBF, while release of endothelin (endothelium-derived contracting factor "EDCF") causes vasoconstriction. It has 3 isoforms (ET-1, ET-2, and ET-3). An increase in the metabolic rate such as in pain, anxiety and convulsions increases CBF, and a decrease in the metabolic rate as with hypothermia, barbiturates and diazepam decreases CBF; therefore, regional CBF parallels the metabolic activity.

(II) Extrinsic Mechanisms:

CBF is affected by the following factors:

1- Respiratory Gas Tension:

a- $PaCO_2$: (the most important): CBF is **directly** proportionate to $PaCO_2$ between tensions of **20-80 mm Hg** i.e., increased $PaCO_2$ causes cerebral vasodilation which increases CBF and ICP, and decreased $PaCO_2$ causes cerebral vasoconstriction which decreases CBF and ICP. CBF changes ≃ 1-2 mL/100 g/min (1-2%) per one mm Hg change in $PaCO_2$. Beyond this range i.e., when $PaCO_2$ is < 20 mm Hg, maximal cerebral vasoconstriction occurs or when it is > 80 mm Hg, maximal cerebral vasodilation occurs. Therefore, little effects on CBF take place (figure 15-6).

Mechanisms: A change in $PaCO_2$ causes an immediate effect on CBF because CO_2 crosses blood brain barrier easily and causes a change in pH of cerebrospinal fluid and cerebral tissues. The change in pH of cerebrospinal fluid is the main factor affecting CBF; therefore, $PaCO_2$ acts via changes in H^+ ions.

After 24-48 hours from the change of CBF due to the changes of $PaCO_2$, HCO_3^- in CSF tries to compensate for the effect of $PaCO_2$ causing a decrease in $PaCO_2$ effect on CBF. This compensation cannot be immediate because HCO_3^- cannot cross blood brain barrier (blood brain barrier is impermeable to ions).

N.B.: During head injury, mild hyperventilation is needed to decrease $PaCO_2$ to 30-35 mm Hg. This causes cerebral vasoconstriction which decreases ICP; therefore, there is no need for aggressive hyperventilation which produces severe vasoconstriction. This causes harmful effect on the already compromised brain.

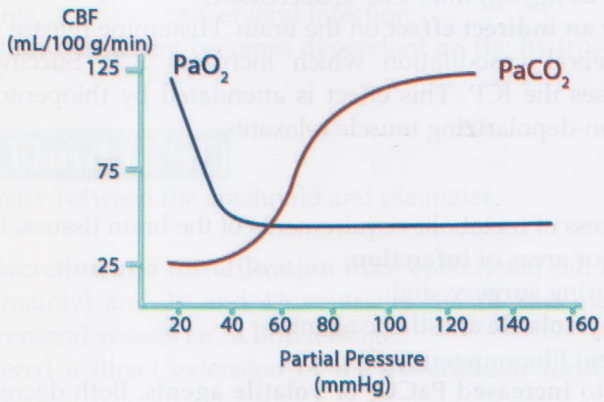


Figure 15-6: The effect of $PaCO_2$ and PaO_2 on CBF

b- PaO_2: A change in PaO_2 **below 50 mm Hg** causes a marked change in CBF **inversely** while a change in PaO_2 above 50 mm Hg causes a little change in CBF inversely.

The combination of arterial hypoxemia and hypercarbia exerts a synergistic effect, with increases in CBF that exceed the increase that would be produced by either factor alone.

2- Extracellular pH (H^+ ions):

H^+ ions in extracellular fluid cannot cross blood brain barrier; so, they have a little effect on CBF e.g., acute metabolic acidosis.

3- Temperature:

CBF varies **directly** with temperature where CBF changes 5-7% per °C. Increased temperature causes vasodilation which increases CBF and cerebral metabolic rate (CMR) up to 42 °C where CMR is decreased due to cell damage. Decreased temperature causes vasoconstriction which decreases CBF (and CMR). At 20 °C, EEG becomes isoelectric.

4- Blood Viscosity: is mainly determined by hematocrit (Hct). Hct between **30-50%** has **a little effect** on CBF. Beyond these limits, CBF varies inversely with Hct. Hct < 30% increases CBF as that occurs with cardiopulmonary bypass, but this also decreases O_2 carrying capacity of blood, while Hct > 50% decreases CBF as that occurs with marked polycythemia.

Effect of Anesthetic agents on CBF (and Other Cerebral Physiology)

- All **inhalational agents**:
  - decrease CMR especially isoflurane, desflurane and sevoflurane.
  - increase CBF, cerebral blood volume, and ICP. The least increase in CBF occurs by **isoflurane and sevoflurane; therefore,** they are **of choice** in patients with decreased intracerebral compliance. Therefore, on large doses such as > 1 MAC for halothane and isoflurane and > 1.5 MAC for sevoflurane), autoregulation is abolished.

Central nervous actions of inhalational anesthetic agents are discussed in the chapter of "Pharmacology of Anesthesia & Intensive Care".

- All **i.v. agents**:
  - decrease CMR especially thiopentone and etomidate.
  - decrease CBF, cerebral blood volume and ICP especially **thiopentone**; therefore, it is **of choice** in patients with decreased intracerebral compliance, and with the exception of **ketamine**, it increases them; so, it **is contraindicated.**

- **Fentanyl** decreases ICP. It is **of choice** in decreased intracerebral compliance.
- Other drugs:

1- Vasopressors: With normal autoregulation, they increase CBF only if mean arterial pressure is beyond 150 mm Hg. In the absence of autoregulation, they increase CBF by their effect on cerebral perfusion pressures.

2- Vasodilators: increase CBF and cerebral blood volume which in turn increase the ICP, except trimethaphan and α blockers which have little or no effect.

3- Dopamine: at doses of < 2 μg/kg/min, little or no effect on CBF is present,
at doses of 2-6 μg/kg/min, CBF is increased,
and at doses of 7-20 μg/kg/min, CBF is decreased.

4- **Muscle Relaxants:** have **an indirect effect** on the brain. Histamine release produced by some muscle relaxants may cause cerebral vasodilation which increases ICP. Succinylcholine causes cerebral vasodilation which increases the ICP. This effect is attenuated by thiopentone, hyperventilation, and defasciculating doses of non-depolarizing muscle relaxants.

N.B.:

Luxury Perfusion:

It is an increase of CBF in excess of metabolic requirements of the brain tissues. It is observed in:

- tissues around **tumors** or areas of **infarction**,
- tissues manipulated during **surgery**, and
- patients anesthetized by **volatile** anesthetic agents.

Intracerebral Circulatory Steal Phenomenon:

It is a paradoxical response to **increased $PaCO_2$ or volatile agents.** Both decrease CBF to ischemic areas and increase CBF to normal areas of brain. Arterioles in ischemic areas are already maximally vasodilated (and unreactive); they cannot dilate further in response to increased $PaCO_2$ or volatile agent.

Inverse Steal or Robin Hood Phenomenon:

It is a paradoxical response to **decreased $PaCO_2$ or barbiturates.** Both increase CBF to ischemic areas and decrease CBF to normal areas of brain. Arterioles in ischemic areas remain maximally vasodilated (and unreactive), while in normal areas they will vasoconstrict producing blood redistribution from normal to ischemic areas.

Blood Brain Barrier (BBB)

The BBB is formed of the junctions between the vascular endothelial cells which are nearly fused (i.e., pores are very rare and tight if present). This produces a lipid barrier which allows passage of lipid soluble substances only (figure 15-7).

Factors Affecting Passage of Substances:

1- Size: **Small sized** substances pass more easily.

2- Charge: **Unionized** substances pass more easily.

3- Lipid solubility: **Lipid soluble** substances pass more easily.
4- Degree of protein binding: **Free** substances pass more easily.
For example:
- Substances freely passing the BBB are CO_2, O_2 and lipid soluble substances such as most anesthetics.
- Substances poorly passing the BBB are ions, proteins and large substances such as mannitol.

Water freely passes BBB by **bulk flow.** Movement of the water is affected by the osmotic pressure. Acute hypertonicity of the plasma allows water to pass out of the brain, while acute hypotonicity of the plasma allows water to pass into the brain. These effects are short lived as Na^+ equilibration occurs within 2-4 hours, but when the changes of osmolarity are marked and acute, fluid shifts rapidly to the brain resulting in marked abnormalities of serum Na^+ or glucose which should be corrected slowly.
N.B.: Mannitol, an osmotically active substance does not cross BBB; therefore, it decreases the brain volume.

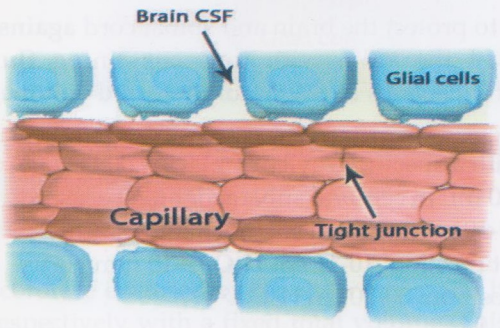


Figure 15-7: Blood brain barrier

Disruption of BBB is caused by:

- Hypoxia.
- Head trauma.
- Severe hypertension.
- Sustained seizures.
- Marked hypercapnia.
- Head tumors.
- Cerebral strokes.
- Cerebral infection.

Under these conditions, fluid movement becomes dependant on the hydrostatic pressure rather than the osmotic pressure.

Cerebro-Spinal Fluid (CSF)

It fills the subarachnoid space between the arachnoid and pia mater.

Formation:

CSF is formed by **active secretion and ultrafiltration** from ependymal cell lining of **choroid plexuses** in the **2 lateral ventricles** (mainly) and 3rd and 4th ventricles. Small amounts of CSF leak into the peri-vascular spaces from the cerebral vessels i.e., a BBB leakage.
Therefore, CSF is considered a direct extension of the extracellular fluid compartment of the central nervous system.
The rate of CSF production in adult is **0.3-0.5 mL/min**.

Circulation:

CSF passes from the **2 lateral ventricles** through **foramen of Monro** to the **3rd ventricle**. Then, CSF passes via **aqueduct of Sylvius** to the **4th ventricle**. CSF then enters **the cerebro-medullary cistern** (Cisterna Magna) through 3 foramina in the roof of the 4th ventricle; **median foramen of Magendie** and **two lateral foramina of Luschka.** CSF then passes to the subarachnoid space.
This circulation does not take part in spinal analgesia.

Absorption:

1- CSF is absorbed via **microscopic arachnoid villi** and **macroscopic arachnoid granulations** in the subarachnoid space into venous sinuses of the brain as the arachnoid mater invaginates into large venous sinuses (figure 15-8).
Although the mechanism remains unclear, absorption appears to be directly proportionate to intracranial pressure and inversely proportionate to cerebral venous pressure.
2- Some CSF is absorbed around spinal nerves into spinal veins.

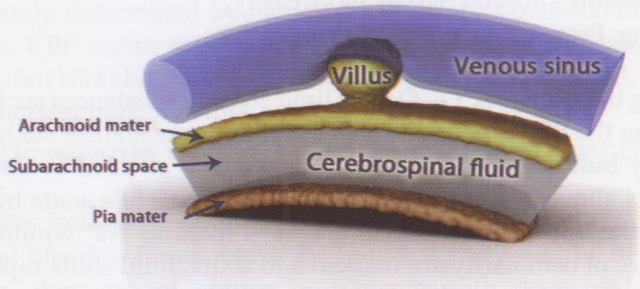


Figure 15-8: CSF absorption

Functions:

- It acts as a **water suspension** to protect the brain and spinal cord **against trauma**.
- It surrounds certain parts of the brain **with ions containing fluid;** so, changes in CSF HCO_3^- concentrations are responsible for changes in respiratory rate and volume mediated by **chemoreceptors.**

Physical Properties:

- It is a clear, colorless fluid, with a specific gravity of 1.003- 1.009 (1.006) at 37 °C.
- Volume: total **125-150 mL;** 100 mL in cerebral subarachnoid space and
  25-50 mL in spinal subarachnoid space.
- Pressure: in lateral recumbent position: **10-15 cm H_2O** (7-10 mm Hg).
  in sitting or erect position: 30-50 cm H_2O.

Chemistry: It is protein-free plasma.

	Plasma (mmol/L)	CSF (mmol/L)	Remarks
PH	7.4	7.4	The same as plasma.
Osmolarity	300	300	Isotonic or slightly hypertonic
Na^+	142	144-152	Higher than plasma.
Cl^-	105	123-128	Cl^- is very high in CSF because CO_2 passes into glial cells where by the action of carbonic anhydrase enzyme it is hydrated to carbonic acid which dissociates into HCO_3^- and H^+. The resulting HCO_3^- ions are exchanged for Cl^- that passes into the CSF against a concentration gradient (figure 15-9).
Glucose (fasting)	4	2.5-4.5	Lower than plasma.
K^+	5	2.0-3.0	Lower than plasma.
Ca^{++}	3	1.1-1.3	Lower than plasma.
HCO_3^-	28	22-30	Lower than plasma.
Urea	3	2.0-7.0	Lower than plasma.
Protein	60-80 g/L	0.2-0.4 g/L	Protein is very low because it only leaks from vessels into peri-vascular fluid

Drugs Decreasing CSF Production:

- Carbonic anhydrase inhibitor (acetazolamide).
- Spironolactone.
- Furosemide.
- Vasoconstrictors.
- Corticosteroids.
- Isoflurane.

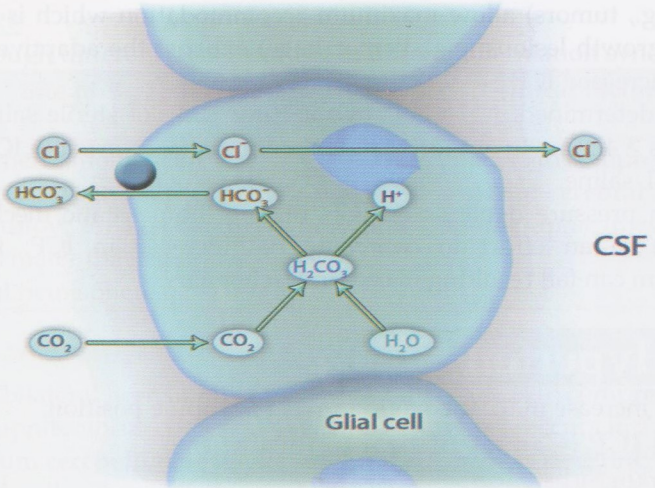


Figure 15-9: Chloride movement inside the glial cells

Intracranial Pressure (ICP)

Monro-Kellie Hypothesis

Normally, the brain and spinal cord are enclosed by the dura mater and bone in a rigid closed "box"; the cranial vault and spinal canal respectively with a fixed total volume. This is true except in neonates and infants where the sutures are not yet fixed. The cranial vault consists of:

- Brain tissues (1500 g) 80% (24% solid and 56% water).
- Blood (150 mL) 12%.
- CSF in cerebral subarachnoid space (100 mL) 8%.

The pressure within this closed space is referred to as the intracranial pressure (ICP). Any increase in one component must be offset by an equivalent decrease in another to prevent a rise in ICP.

Value: Normally ICP is **5-15 mm Hg.**

It has normal respiratory swings because it is related directly to intrathoracic pressure.

Intracranial Compliance: (Δ volume / Δ pressure)

(Volume-Pressure Relationship)

Small increase in intracranial volume causes minimal increase in ICP (area 1 to 2) due to the following adaptive mechanisms (figure 15-10):

- Initial redistribution of CSF from cranial to spinal subarachnoid space.
- Increased CSF absorption and decreased CSF production.
- Decreased total cerebral blood volume especially venous blood.

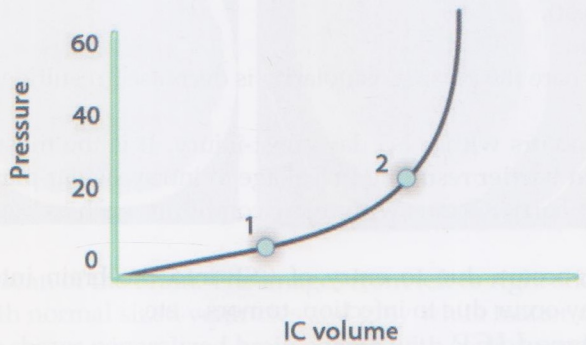


Figure 15-10: Intracranial compliance

More increase in intracranial volume causes a great increase in ICP (beyond the point 2 "point of decompensation" on the curve). The curve becomes steep with loss of compliance due to exhaustion of adaptive mechanisms. The increase in ICP may cause herniation of the brain.

Slow growth lesions (e.g., tumors) allow maximum accommodation which is relatively associated with normal ICP, but rapid growth lesions (e.g., hemorrhage) exhaust the adaptive mechanisms rapidly and are associated with an increased ICP.

The compliance can be determined in patients by injecting 1 mL of sterile saline via an intraventricular catheter. If ICP increases > 4 mm Hg, it indicates poor compliance. Normally ICP changes less than 2 mm Hg with injection of 1 mL saline.

Since cerebral perfusion pressure depends on ICP, initially homeostatic mechanisms work to increase mean arterial pressure in an effort to overcome the increase in ICP; however eventually, this compensatory mechanism can fail resulting in cerebral ischemia.

Intracranial Hypertension

Definition: Sustained increase in ICP above 15 mm Hg in supine position.

Causes of Increased ICP (Causes of Brain Herniation)

A) Causes Increasing Brain Substances:

- Intracerebral **abscess**.
- Intracerebral **tumors**.
- Intracerebral **hematoma** such as stroke or head trauma.

N.B.: Intracerebral hematoma or tumor increases ICP by one of three mechanisms:

- Directly due to their size.
- Indirectly by causing obstruction to CSF outflow.
- Indirectly by causing edema in normal surrounding brain tissues.

B) Causes Increasing Blood Volume:

- Increased CBF (cerebral vasodilators) as with **hypoxia, hypercarbia, Na^+ nitroprusside, or volatile anesthetics**.
- **Hypotension with intact autoregulation**; it causes vasodilation of cerebral vessels to maintain CBF (i.e., autoregulation) unlike hypertension which causes vasoconstriction of cerebral vessels to maintain CBF by autoregulation.
- **Hypertension with impaired autoregulation** because CBF becomes pressure dependent.
- Increased cerebral venous volume as with increased **intrathoracic pressure, venous obstruction** in the neck, **head down tilt, coughing, straining**, and positive end-expiratory pressure (**PEEP**).

C) Causes Increasing CSF Volume:

- CSF outflow obstruction such as obstructive hydrocephalus.
- Infection such as meningitis or encephalitis (leading to brain edema or CSF outflow obstruction).
- Benign intracranial hypertension.
- **Brain Edema**: is defined as an increase in the water content of the brain. It is three types:

  1- Cytotoxic Edema: It occurs within minutes of ischemia. It occurs due to influx of ions into brain cells with failure of brain cells to actively extrude Na^+. This causes an uptake of water from the extracellular space with progressive cellular swelling. It usually occurs due to metabolic insults such as
  - hypoxia (cardiac arrest),
  - ischemia (stroke), and
  - water intoxication where the plasma osmolarity is decreased resulting in movement of water into the cells.

  2- Vasogenic Edema: It occurs within 2-3 days post-injury. It is the most common. It occurs due to **disruption of blood brain barrier** resulting in leakage of intravascular plasma proteins into the brain. Disruption of blood brain barrier occurs with many conditions such as hypoxia, hypercarbia…etc (see above).

  3- Interstitial Edema: It occurs due to entry of CSF into the brain interstitium as in obstructive hydrocephalus which may occur due to infection, tumors…etc.

Clinical Picture of Increased ICP

a- Early: It is asymptomatic then, headache, vomiting with or without nausea (effortless vomiting), papilloedema, or unilateral pupillary dilatation occurs.

b-Late:
- focal neurological lesions according to the herniation site (see below),
- a change in the level of consciousness up to coma due to reduced cerebral perfusion.

and/or
- irregular ventilatory pattern.

Herniation Syndromes

The brain can herniate through different sites resulting in different herniation syndromes (figure 15-2):

Herniation Syndrome	Site of Brain Herniation	Clinical Picture and Complications
1- Subfalcine Herniation	Due to herniation of **cerebral hemispheric contents** (the cingulated gyrus) **under the falx cerebri** (a reflection of dura mater that separates the two cerebral hemispheres).	It leads to compression of branches of the **anterior cerebral artery** and is evident on radiographic imaging as midline shift.
2- Transtentorial Herniation **a- Bilateral**	Due to bilateral herniation of the temporal lobe (supratentorial contents) **over the tentorium cerebelli** (a reflection of dura mater that lies rostral to the cerebellum and makes the border between the supratentorial and infratentorial spaces).	It leads to compression of **brainstem** which occurs in a rostral to caudal manner resulting in altered consciousness, defects in gaze, afferent ocular reflexes, and, finally hemodynamic and respiratory compromise followed by death.
b- Unilateral (Uncal Herniation)	Due to unilateral herniation of the **uncus** (i.e., the medial portion of the temporal lobe) **over the tentorium cerebelli**.	It leads to compression of the **oculomotor nerve** against the brainstem resulting in pupillary dilatation, ptosis, and lateral deviation of the affected eye, which occur prior to evidence of brainstem compression and death.
3- Tonsillar Herniation	Due to herniation of the **cerebellar tonsils through the foramen magnum**.	It leads to **medullary** compression with compression of vital centers including cardio-respiratory instability and subsequent death.
4- Herniation through a Traumatic Defect	Due to herniation of **any superficial brain tissues** through a **traumatic defect** in the cranial cavity.	It leads to a clinical picture that differs according to the part of the brain herniated.

Investigations:

1- Computerized tomography (CT scan) (figure 15-11).

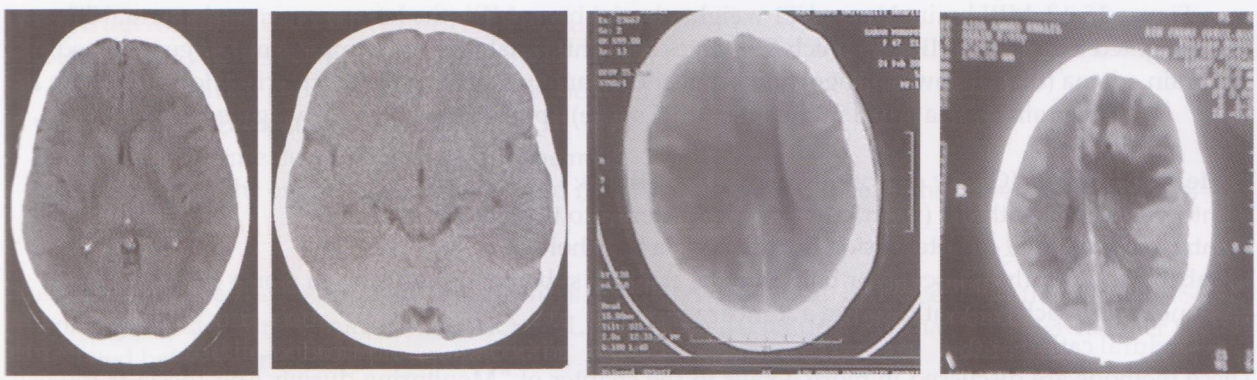


Figure 15-11: CT scan of the brain. The images from left to right show; the first image is normal with normal sized ventricles and grey white matter differentiation. The second image shows generalized brain edema with compressed ventricles and lost grey-white matter differentiation. The third and fourth images show perifocal edema around a brain tumor with compressed ipsilateral ventricle and midline shift to the opposite side (i.e., mass effect)

2- Magnetic resonant imaging (MRI) (figure 15-12).

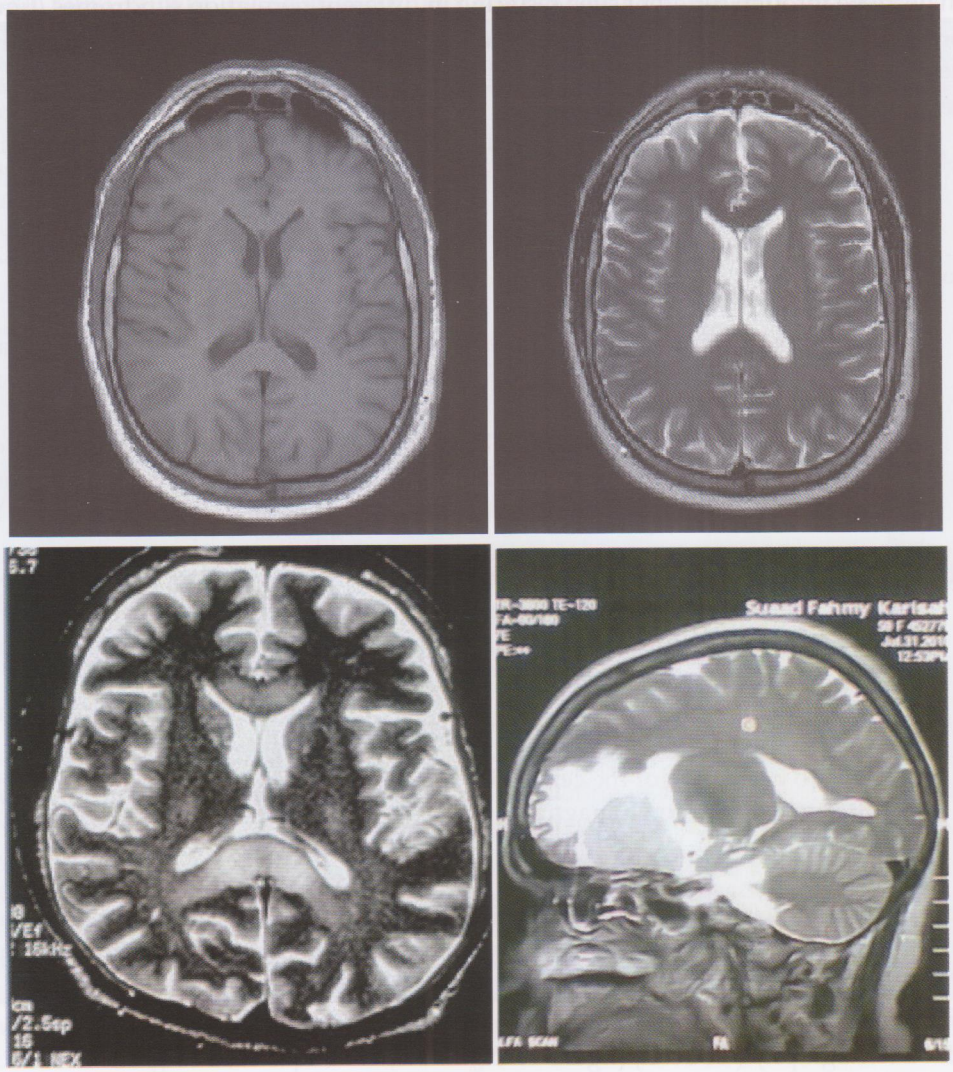


Figure 15-12: MRI brain. Normal T1 weighted axial brain MRI (the left upper image), normal T2 weighted axial brain MRI on which CSF gives a bright signal (the right upper image), generalized brain edema (the left lower image) and brain edema around a brain tumor (the right lower image). The brain edema (fluid in the interstitial space) appears bright on T2 weighted MRI.

3- **Measurement of ICP:** by one of the following methods:

1- Intraventricular catheter (ventriculostomy catheter) into the lateral ventricle.
2- Intra-parenchymal catheter inside the brain via a burr hole.
3- Subarachnoid catheter (screw or bolt) into the cerebral subarachnoid space via a burr hole.
4- Lumbar subarachnoid catheter via a lumbar puncture.
5- Extradural catheter.

These methods are discussed in more details in the chapter of "Monitoring during Anesthesia & Intensive Care".

Plateau waves are abrupt increases in ICP to as high as 100 mm Hg observed during continuous monitoring. During this increase in ICP, patients may become symptomatic of inadequate cerebral perfusion and spontaneous hyperventilation or a change in mental status may occur. Anxiety and painful stimulation can initiate abrupt increases in ICP.

Treatment of Increased ICP:

The usual recommendations are to treat any sustained increase in ICP that:

- exceed 20 mm Hg or
- less than 20 mm Hg, but with occasional plateau waves.

A) Treatment of the Underlying Cause:

B) Reduction of ICP:

1- Fluid Restriction:

Amount: **1/2 - 1/3 the usual daily requirement** of fluids (i.e., 1000-1500 normal saline) is administered.

Value of Fluid Restriction:

1- It increases the osmotic effects (and decreases hypervolemia produced by mannitol).
2- It facilitates induced hypotension.
3- It decreases the incidence of postoperative cerebral edema.

Type: **Avoid dextrose 5%** solution because dextrose will enter inside cells to be metabolized leaving the water intravascular which in turn decreases plasma osmolarity and increases movement of the water from the plasma into brain cells resulting in brain edema and increased ICP, as well as, the harmful effect of hyperglycemia on the brain as it increases cerebral acidosis and recruitment of inflammatory cells, free radical formation, and endothelial dysfunction.

2- Moderate Hyperventilation:

Aim: to keep **$PaCO_2$** in the range of **36-40 mm Hg** i.e., to maintain **normocapnia.**

In acute increases of ICP, $PaCO_2$ can be reduced to **30-35 mm Hg transiently** then returned to the normal range. The effects of reduced $PaCO_2$ (between 30-35 mm Hg) will diminish with time and wane after 6-12 hours. When prolonged hyperventilation is discontinued, rebound increase in ICP is a potential problem, especially if normocapnia is rapidly restored.

Mechanisms: The reduction of $PaCO_2$ results in:

- Compensatory respiratory alkalosis against the acidosis of ischemia i.e. increased intracellular and extracellular pH.
- A decrease in cerebral blood volume which in turn decreases ICP.
- Vasoconstriction in non-ischemic areas which in turn causes redistribution of the blood to ischemic areas (i.e., inverse steal phenomenon).

Precautions:

- Avoid hypocapnia because it causes severe cerebral vasoconstriction which increases cerebral ischemia.
- Avoid hypercapnia because it causes steal phenomenon in focal ischemia. It worsens intracellular acidosis and increases ICP.

3- Reduction of Cerebral Venous Pressure:

Avoid cerebral venous pressure elevation by:

- Head-up position about 30 degrees above the level of the heart.
- Avoiding coughing and straining.
- Avoiding extreme flexion or twisting of the neck.
- The tape from the endotracheal tube should not cross the jugular area (if the patient is intubated).

4- Cerebral Dehydrating Measures:

a- Hyper-Osmolar Agents (Osmo-Diuretics):

They increase plasma osmolarity which shifts the fluid from the brain cells to the plasma. Serum osmolarity should be maintained < 320 mOsm/L to avoid renal failure. A urinary bladder catheter should be inserted before therapy.

1- **Mannitol 10, 20,** and **25%.**

Mannitol is of choice. It can remove about 100 mL of water from the patient's brain.

Dose: **0.25-0.5 g/kg** infused **over 10-20 min** initially. If the desired effect is not achieved, either administer another dose with a maximum 4 g/kg/day or use another type of therapy. Some authors recommend a higher dose from the start 1 g/kg.

Onset: 10-15 min with maximum effect 1 hour.

Duration: 2 hours.

Advantages:

- It is less irritant than urea.

- It causes less rebound increase in brain volume than urea.
- It makes the brain softer and more easily retractable.

Disadvantages:

1. **Transient hypervolemia** may occur; therefore, it is contraindicated in congestive heart failure or in patients with impaired renal function and it may increase surgical bleeding.
2. When intracerebral hematoma is suspected, mannitol may shrink healthy brain tissues leading to **expansion of intra- and extra-cerebral hematomas**; therefore, it is contraindicated in cerebro-vascular lesions such as intracerebral aneurysm, arterio-venous malformation (AVM) until the cranium is opened.
3. Excessive mannitol usage may cause excessive fluid loss resulting in **hypotension** that may affect adequacy of cerebral perfusion pressure.
4. Excessive mannitol usage may draw water from the heart cells producing **irreversible cardiac arrest**; therefore, it is contraindicated in cardiac arrest.
5. **Vasodilation** which may cause:
   - Intracranial vasodilation that increases CBF and ICP in patients with normal ICP, but mannitol will not further increase ICP in patients with intracranial hypertension.
   - Extracranial vasodilation that causes hypotension.

   This vasodilation occurs especially in rapid infusion of mannitol 25%, but very rarely in slow infusion of mannitol 10-20%.
6. In elderly patients, if given rapidly, it may cause **subdural hematoma** due to rupture of bridging veins entering the sagittal sinus.
7. If it is used **> 4 days or if there is a damaged blood brain barrier**, mannitol may cross the blood brain barrier causing **rebound effects** with increased brain size; therefore, it is contraindicated in vasogenic brain edema.
8. On prolonged use, mannitol produces:
   - Electrolyte depletion especially K^+ requiring careful monitoring and replacement.
   - Increased plasma osmolarity that may exceed 320 mOsm/L, producing neurological and renal dysfunction (acute tubular necrosis); therefore, its prolonged use should be avoided.

N.B.: Oral glycerol and isosorbide are preferred for chronic IC hypertension.

2- **Hypertonic Saline 3% or 7.5%:** In refractory cases.

Effect:

- Hypertonic saline is a volume expander in the systemic circulation and does not impair renal function as seen with mannitol. More details are discussed in hypovolemic shock in the chapter of "Cardiovascular Disease".
- As compared with mannitol, hypertonic saline produces better control of ICP, but no change in mortality and neurologic outcome is observed; therefore, it is not yet recommended as a standard of management in patients with head trauma or increased ICP.

Dose:

- A **3% saline** is used at a rate of **75-150 mL/hour**, whereas a bolus of 250 mL may be given for aggressive therapy.
- A **7.5% saline** is used at a dose of **2 mL/kg** i.v. slowly.

3- **Urea 30%:**

Dose: 1-1.5 g/kg infused over 60 min.

Disadvantages:

- It is very irritant to veins.
- Rebound increase in brain volume may occur.

4- **Glycerol 10%:**

Dose: 0.5-1.0 g/kg i.v. or oral.

5- **Isosorbide.**

b - Diuretics:

Loop diuretics as furosemide (1 mg/kg, with onset 2-10 min).

Diuretics are of choice in patients with congestive heart failure and renal impairment.

Action:

- Diuresis causes brain dehydration.
- Diuretics decrease CSF formation and brain edema.

N.B.: Combined osmotic and loop diuretics cause a synergistic effect, but require close monitoring of s. K^+.

c- Steroids: **(Dexamethasone or Methylprednisolone)**

Steroids are effective in: • localized cerebral vasogenic edema surrounding intracerebral tumors, and
• benign intracranial hypertension (pseudotumor cerebri).

Steroids are not effective in focal or global ischemia, or head trauma.

Dose:

Dexamethasone 10 mg i.v. followed by 4 mg im/6 hours.

Action: Steroids needs 12-36 hours to decrease ICP.

- It causes simple brain dehydration.
- It promotes repair of the blood brain barrier; so, it is used in vasogenic brain edema.
- It acts as a free radical scavenger and inhibits lipid peroxidation reactions producing a decrease in free fatty acid accumulation.
- It stabilizes capillary membranes.
- It decreases CSF production.

Disadvantages:

- It increases blood glucose level which may adversely affect the outcome if ongoing cerebral ischemia.

5- Drugs Increasing Cerebro-Vascular Resistance:

These drugs cause cerebral vasoconstriction which decreases CBF and ICP especially in head trauma such as **lidocaine, thiopentone, or propofol infusion** (care should be taken with the latter in pediatric patients due to the drug-associated metabolic acidosis which may be fatal).

6- Hypothermia:

Mild degree of hypothermia is usually chosen (up to 34 °C). Hypothermia is indicated in surgeries on cerebral vasculature that requires long periods of cerebral ischemia.

Action: Decreasing brain temperature causes: • Decreased brain metabolism, CBF, and ICP.
• Decreased CSF formation.

7- Measures Decreasing CSF Volume:

a- In Acute Conditions or intraoperatively, aspiration of CSF may occur through:

- **A ventricular tap (or ventriculostomy catheter)**.
- **A lumbar subarachnoid drainage** (by a rate < 5 mL/min).

Disadvantages: If a higher rate is drained, the following side effects may occur:

- Arterial hypertension and dysrhythmia (bradycardia and Cushing reflex).
- A rebound increase in ICP.
- Brain herniation and medullary coning.

b- In Chronic Conditions:

A shunting procedure is preferred either to: • the right atrium (ventriculo-atrial shunt), or
• the peritoneal cavity (ventriculo-peritoneal shunt).

c- Decreasing CSF Production is done also by:

- Carbonic anhydrase inhibitors such as acetazolamide (*Diamox*).
- Diuretics.
- Hypothermia.

8- Surgical Bony Decompression:

Ii is performed in resistant cases.

Central Nervous System Protection

It includes: • Brain protection.
• Spinal Cord protection: discussed later in the chapter of "Anesthesia and Vascular Surgery".

Brain Protection

Pathophysiology of Cerebral Ischemia

The strategies for brain protection are based on the understanding of the pathophysiology of cerebral ischemia. Cerebral ischemia is either global or focal.

A) Global Ischemia:

• All neurons in the brain are affected by ischemia, but not all neurons have the same vulnerability to ischemia. The most susceptible neurons to ischemia are called **selectively vulnerable neurons**. They include: ▫ Hippocampus.

- Layer three of the cerebral cortex.
- Striatum.
- Purkinje cells of the cerebellum.

• Global ischemia may result from conditions such as cardiac arrest, severe respiratory failure, severe shock, near-drowning, severe hypoglycemia, or asphyxia (such as during anesthetic faults "esophageal intubation").

• After restoration of CBF, two conditions may occur:
- **Reactive hyperemia**: where CBF shows a transient increase above basal levels.
- **Post-ischemia hypoperfusion**: where CBF shows a reduction up to 50% of basal levels which may persist for a variable period after reperfusion contributing to neuronal injury.

B) Focal Ischemia:

• It affects certain areas of the brain due to a condition such as head trauma or injury, vascular stenosis (atherosclerosis), vascular occlusion (embolism), or vascular spasm (hemorrhage).

• The region supplied by end arteries shows rapid death of brain tissues and is called the **core.**

• Surrounding the core is a variable area of the brain called the **ischemic penumbra**. This area is slightly ischemic. This slight ischemia makes the brain tissue in this area electrically silent with marked functional impairment, but has not yet undergone ischemic depolarization (figure 15-13).

In the penumbra, there is a gradual decline in neuronal adenosine triphosphate (ATP) levels. The penumbra is viable for several hours and can be salvaged by flow restoration. If reperfusion is not established, the penumbra is gradually recruited into the core (i.e., more brain infarction).

• Cytotoxic, followed by vasogenic brain edema occurs after brain ischemia.

• **The process of healing** occurs over a period of several weeks (**4-6 weeks**). Necrotic tissue is gradually resorbed and the resulting cystic cavity is lined by a glial scar. In the region of the brain surrounding the infarction, autoregulation and CO_2 reactivity are re-established within 4-6 weeks.

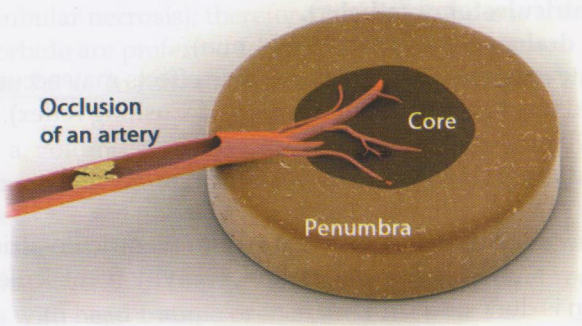


Figure 15-13: Focal ischemia

Ischemic Cascade

• The brain is very vulnerable to ischemic injury because of its relatively high O_2 consumption and near-total dependence on aerobic glucose metabolism. Interruption of cerebral perfusion, deficiency of metabolic substrate (glucose), or severe hypoxemia rapidly results in functional impairment. If these conditions are not reestablished within 3-8 minutes under most conditions, anaerobic glycolysis, ischemic cascade and depletion of ATP stores begin resulting in irreversible neuronal injury.

• Ischemic cascade passes into two main stages:

a- Stage of Tissue Acidosis:

With prolonged ischemia, **anaerobic glycolysis** is activated with production of **lactic acids (metabolic lactic acidosis)**. Anaerobic glycolysis is inadequate to maintain cellular energy stores of ATP because the brain depends mainly on aerobic glycolysis. This leads to **depletion of ATP** with failure of ATP dependent membrane ion pumps such as Na^+-K^+ ATPase pump and Ca^{++} pumps. This leads to influx of Na^+ and Ca^{++} and efflux of K^+.

Lactic acidosis and depletion of ATP result in **increased cellular membrane permeability** and **cellular edema**.

Hyperglycemia produces a more harmful effect because it provides a greater amount of substrate for anaerobic glycolysis and; therefore, more acidosis than that with normoglycemia occurs. Therefore, more ischemia occurs with hyperglycemia.

All the above events lead to terminal membrane depolarization with release of the excitatory neurotransmitters after which the ischemic cascade enters the second stage.

b- Stage of Excitotoxicity:

Terminal membrane depolarization leads to excessive release of **excitatory neurotransmitters** such as glutamate and aspartate. These excitatory neurotransmitters cause stimulation of two main events; tissue necrosis and apoptosis.

1- Tissue Necrosis:

- The excitatory neurotransmitters stimulate N-methyl D-aspartate (**NMDA) receptors**, α-*a*mino-3-hydroxy-5-*m*ethyl 4-isoxazole*p*ropionic *a*cid **(AMPA) receptors**, and voltage dependent Ca^{++} and Na^{+} channels leading to **increased Ca^{++} and Na^{+} influx** up to toxic levels. These changes stimulate **catabolic intracellular processes** including enzymes as proteases and **phospholipase A_2**. The latter enzyme acts on cell membrane releasing **arachidonic acid** which is metabolized by **cyclo-oxygenase and lipo-oxygenase enzymes**. Therefore, **prostaglandins and leukotrienes** are produced which in turn evoke inflammation. Ischemia induces **inflammation** by expression of adhesion molecules "Intercellular Cell Adhesion Molecule" (ICAM) and "Vascular Cell Adhesion Molecule" (VCAM) with help of **pro-inflammatory cytokines** such as interleukins (IL)-1, IL-6, and tumor necrosing factor (TNF) α which lead to **chemotaxis and adhesion of leukocytes** and **aggregation of platelets** to the site of inflammation with resulting **mechanical obstruction and occlusion of microcirculation** and more ischemia.
- Ischemia also **activates COX-2 enzyme** which produces **injurious free radicals (**such as superoxide radicals, hydrogen peroxides, and hydroxyl radicals) **and eicosanoids**. They enhance inflammatory reaction.
- Ischemia activates neuronal nitric oxide synthetase (nNOS) and immunological inducible nitric oxide synthetase (iNOS) resulting in production of a **large amount of NO** (with superoxide anion) which in turn produces peroxynitrites. These products produce damage of cellular proteins, membranes, and DNA with activation of DNA repair enzyme called Poly-ADP ribose-polymerase (PARP). This enzyme utilizes ATP which is already depleted resulting in **exacerbation of ischemia**. Endothelial NOS (eNOS) has vasodilator, anti-inflammatory, and antithrombotic actions which maintain cerebral blood flow and decrease neuronal injury.
- Activated microglia elaborate pro-inflammatory cytokines and free radicals. Both increase injury as above, while inhibition of microglia by tetracycline decreases injury. The activated microglia can be observed even 6 months after ischemia.

2- Apoptosis (Programmed Cell Death) (Cellular Suicidal Program):

- It occurs with moderate degrees of ischemic/hypoxic insult. In the initial stage of apoptosis, neurons do not show histo-pathological or physiological evidence of neuronal damage and provide adequate ATP production and physiological membrane potential. Several days later, the neurons start to degenerate.
- Acidosis, excitatory neurotransmitters, and free radicals stimulate apoptosis by producing **mitochondrial injury** with development of mitochondrial permeability transition which in turn causes depolarization of mitochondrial membranes with **release of cytochrome C** from the inner and outer mitochondrial membranes into the cytoplasm. Cytochrome C activates **death signaling complexes such as calpain and caspases 9 and 3**. Calpain and caspases are interleukin converting enzyme-like proteins (i.e., proteases) which stimulate **proteolytic cleavage of a number of cellular constituents** and produce structural changes of biological membranes, **DNA fragmentation**, with production of small particles containing cell debris called **apoptotic bodies**.
- The main difference between apoptosis and necrosis is that the former is not accompanied with inflammation while the latter is accompanied with inflammation.

Finally, both necrosis (and inflammation) and apoptosis result in **membrane degeneration of vascular and cellular structures** such as cell membrane, nuclear acids, receptors, and enzymes which in turn causes **neuronal necrosis and damage** (figure 15-14).

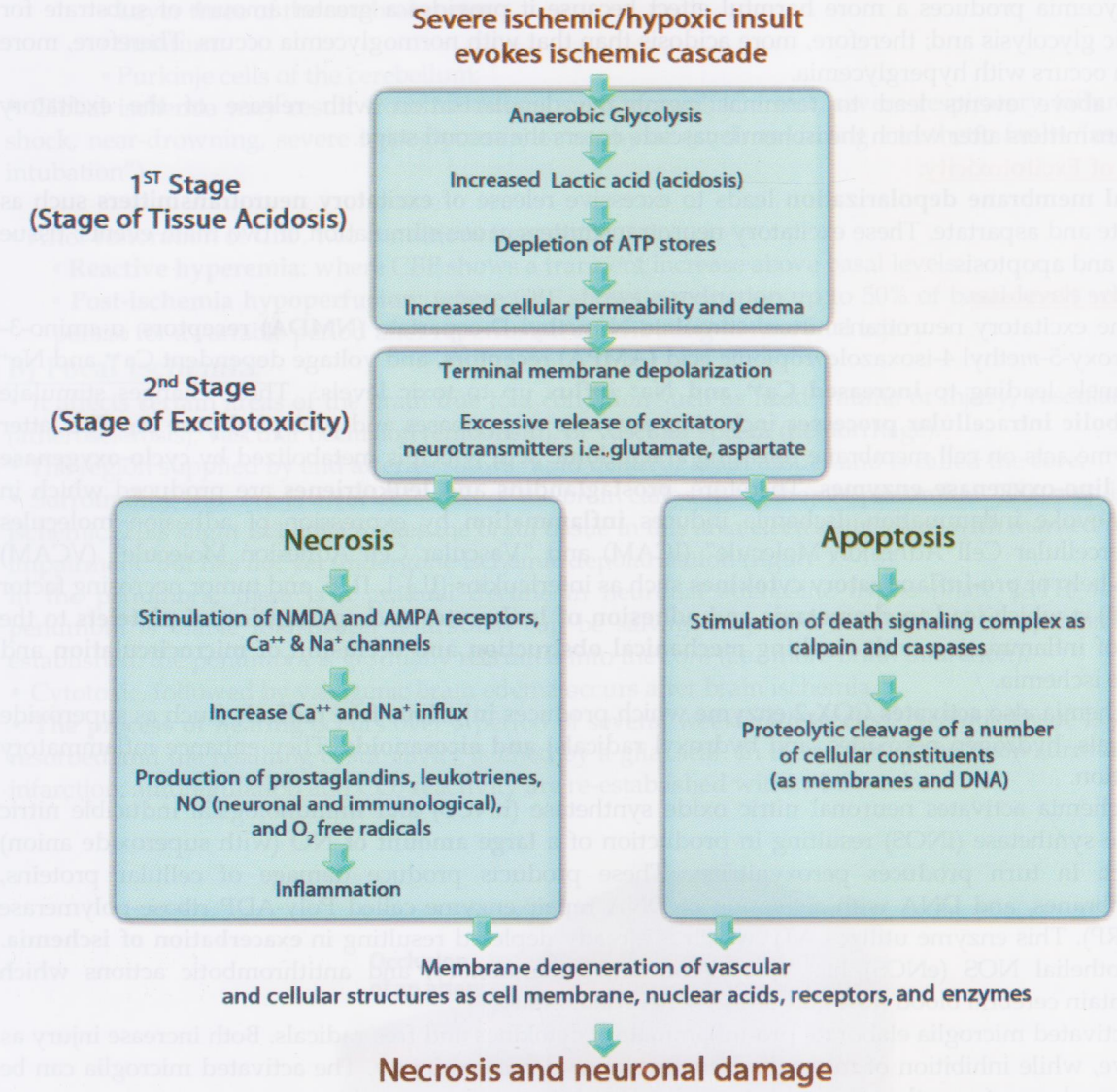


Figure 15-14: Ischemic cascade

The time course of neuronal death is shown in figure 15-15.

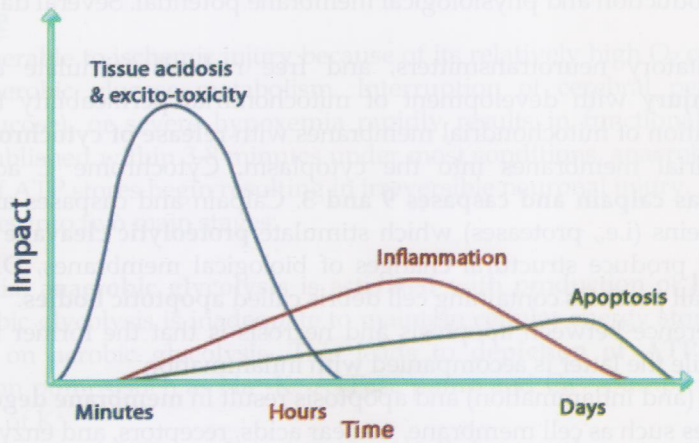


Figure 15-15: Time course of neuronal death

Strategies for Brain Protection

A) Treatment of the Cause of Brain Ischemia:

It is the first line such as supplying O_2 in case of asphyxia, drainage of hematoma, treatment of shock ....etc.

B) General Measures: are beneficial for both **global and focal ischemia.**

1- Keep Normal O_2 Carrying Capacity: by
- keeping hematocrit (Hct) between 30-34% and
- keeping normal PaO_2 levels.

2- Keep Normal blood glucose:

The best blood glucose is **100-150 mg/dL**. It should be measured every 2 hours.

Mechanism: Normoglycemia decreases intracellular lactic acidosis (which occurs with hypo- and hyperglycemia). This maintains normal cellular permeability and decreases cellular edema.

C) Measures Decreasing Cerebral Metabolic Rate of O_2 ($CMRO_2$):

1- Hypothermia: is beneficial for both **global and focal ischemia.**

It is the most effective method for brain protection.

Mechanisms: It decreases all biochemical processes;
- It decreases basal and electrical metabolic rate which in turn decreases CBF and ICP.
- It decreases CSF formation.
- It decreases excitatory neurotransmitter release which in turn decreases Ca^{++} influx.
- It decreases accumulation of lipid peroxidation products and decreases the free radicals.

Methods:

The Optimum Temperature used in brain protection is:
- Mild hypothermia (33-36 °C). It is preferred because it is associated with less side effects.
- Moderate hypothermia (29-32 °C).
- Profound hypothermia (15-28 °C). It is used in selected cases as large giant aneurysm surgery because it increases the toxic metabolites and increases cardiac depression.

Time of Initiation of Hypothermia:
- **For surgery on cerebral vasculature**, prophylactic **intraoperative** hypothermia should be done as recommended by some authors.
- **For head trauma** (it is still controversial); it is done **as early as possible**. The best timing is **within 15-90 min** of insult e.g., in the ambulance. Benefits are still present, if hypothermia is applied 6-24 hours after the initial insult and maintained for 24-48 hours e.g., in intensive care.

Methods of Cooling:

1- **Conventional water circulating cooling blanket**: is ineffective due to poor surface contact with the skin.

2- **A newer external cooling device** has been developed which utilizes **self-adhesive, hydrogel-coated pads** that circulate temperature-controlled water under negative pressure.

3- **Intravascular central venous catheters** are usually used for cooling (and rewarming). These catheters contain special built-in balloons through which cooled or warmed saline is circulated in a closed loop design. The patient's temperature is continuously compared with a target temperature and the controller system is equipped with a safety system that alarms when the temperature is above or below programmed levels or when there is a system malfunction.

Rewarming:

An optimum regimen of rewarming is needed to bring patients to low normothermia to avoid hyperthermic overshoot. This is best done by using a perfusate with a temperature of 2 °C higher than the nasopharyngeal temperature instead of the usual 4-6 °C higher. Most cases die during rewarming.

N.B.: Fever and hyperthermia accentuate excitotoxic release of neurotransmitters, increase production of free radicals, and accelerate cytoskeletal protein degradation. It is now suggested that **prevention of hyperthermia** is associated with **better** results and is essential in all patients. Therefore, hyperthermia in patients with cerebral ischemia should be treated aggressively.

2- Anesthetic Agents: are beneficial for **focal ischemia**.

Mechanism:

They decrease the electrical activity of the brain and potentiate inhibitory neurotransmitters resulting in decreased electrical metabolic rate, but there is no effect on the basal metabolic rate.

a- Volatile Anesthetics: such as isoflurane, desflurane, or sevoflurane (the latter is the best for carotid endarterectomy). They affect different parts of the brain to variable extents.

N.B.: **N_2O is better avoided** due to its neurotoxic effects, **but N_2O is not a contraindication during brain protection** as recent studies have failed to identify the adverse effects of N_2O on the brain. There are many mechanisms which may explain the adverse effects of N_2O:

1- It increases cerebral metabolic rate, CBF, and ICP. These effects occur when N_2O is used alone, but they may be variable if used with other agents.

2- Although N_2O is a NMDA receptor antagonist and decreases excitatory neurotransmitter release (such as glutamate), N_2O also decreases the inhibitory neurotransmitter release (gamma amino butyric acid "GABA"). Therefore, **general dis-inhibition (i.e., stimulation)** occurs which causes neuronal damage. The effects occur with other NMDA receptor antagonists such as ketamine, dextrophan, MK-801…etc; therefore, they are not effective (and may be harmful) in brain protection.

3- It decreases the neuro-protective action of other agents as thiopentone or isoflurane.

4- In patients with folic acid deficiency, single exposure to N_2O can cause spinal cord degeneration.

5- It increases serum homocysteine which increases coagulation and decreases flow-mediated vaso-dilation. Both decrease CBF causing harmful effects.

6- In rats:
- It is neurotoxic as vaculation of both the endoplasmic reticulum and mitochondria in cortical neurons occurs after usage of N_2O.
- N_2O converts non-toxic doses of ketamine into toxic doses.

b- Intravenous Anesthetics:

Thiopentone:

Dose: I.v. infusion of 1-5 mg/kg/hour (i.e., nearly 500 mg "one vial"/hour for adults).

Traditionally, an isoelectric EEG indicating maximal reduction of $CMRO_2$ has been used as the end point for barbiturate administration with the goal of neuroprotection. More recent data demonstrating equal protection after smaller doses have challenged this practice.

Mechanisms of Brain Protection:

1- It decreases electrical activity of the brain resulting in a decrease in the electrical metabolic rate. It has a uniform effect on brain parts (i.e., it increases GABA activity).

2- It has an anticonvulsant action.

3- It blocks NMDA and AMPA receptors resulting in a decrease in Ca^{++} influx.

4- It has an antioxidant action as it inhibits free radical formation.

5- It increases the activity of the hexose mono-phosphate shunt (HMP shunt).

6- It decreases brain edema by producing:
- Peripheral vasodilation that decreases systemic vascular resistance and arterial blood pressure which in turn decreases CBF and ICP.
- Selective cerebral vasoconstriction which decreases CBF and ICP.

7- It is a Na^+ channel and glutamate receptor blocker.

8- It produces inverse steal or Robin-Hood phenomenon where it redistributes blood flow to the ischemic areas (see before).

9- It decreases glucose transfer across the blood brain barrier.

Propofol:

Mechanisms of Brain Protection:

1- Scavenging of free radicals.

2- Inhibition of glutamate release.

3- Prevention of lipid peroxidation.

4- Delaying (but not preventing) apoptotic cell death.

Ketamine:

It blocks the action of glutamate at NMDA receptors, but it produces general dis-inhibition; therefore, it is **not used in brain protection** (see above).

Etomidate is **not used in brain protection** although it has been suggested to produce brain protection because recently it has been proved that the standard **propylene glycol** used in formation of etomidate induces cerebral hypoxia and tissue acidosis leading to harmful effects.

D) Measures Increasing CBF and CPP:

are beneficial for both **global and focal ischemia**.

Two different approaches in the management of CPP attempt to maintain cerebral perfusion at a level adequate to fuel cerebral metabolic needs. There are three concepts that are postulated as follows:

a- Cascade of Cerebral Vasodilation and Vasoconstriction:

1- Rosner Concept:

It needs **intact cerebral autoregulation** as increased CPP produces autoregulatory cerebral vasoconstriction which in turn decreases CBF to return it to normal levels. This decreases intracerebral blood volume and so, it decreases ICP. Therefore, Rosner concept recommends maintaining CPP > 70 mm Hg.

2- Edinburgh Concept:

In patients with an the **autoregulatory curve shifted to the right,** normal CPP and mean arterial blood pressure lie outside the autoregulation range i.e., the perfusion is pressure dependent, but with increased CPP, the arterial blood pressure returns to the autoregulation range. This produces auto-regulatory vasoconstriction that in turn decreases CBF and also causes a decrease in intracerebral blood volume and consequently, it decreases ICP. Therefore, Edinburgh concept also recommends elevation of CPP > 70 mm Hg.

Therefore, according to Rosner and Edinburgh concepts, it is best to **keep CPP within a range of > 65-70 mm Hg** which is achieved by:

1- Mean arterial blood pressure should be **normal or slightly elevated**.

2- Blood viscosity should be **decreased,** although this may decrease O_2 carrying capacity of blood; therefore, the best **Hct is 30-34%.**

3- ICP should be **decreased** as before by the following methods:

- Fluid restriction.
- Moderate hyperventilation.
- Reduction of cerebral venous pressure.
- Cerebral dehydrating measures such as mannitol, furosemide, and glucocorticoid steroids.
- Hypothermia.
- Drugs increasing cerebrovascular resistance as lidocaine, thiopental, or propofol.
- Measures decreasing CSF volume.

The reduction of ICP is discussed in more details above.

b) Lund Concept:

This approach assumes **defective blood brain barrier and cerebral autoregulation.** The Lund concept targets at **low precapillary hydrostatic pressures and cerebral venous constriction** to decrease edema formation and cerebral blood volume. This is achieved by

- Infusion of dihydroergotamine.
- Infusion of α_2 agonists such as clonidine and β_1 antagonists such as metoprolol.
- Normalization of colloidal osmotic pressure.

This approach is less effective than Rosner and Edinburgh concepts.

E) Specific Agents: are used for specific conditions.

1- Ca^{++} Channel Blockers: (Nimodipine and Nicardipine).

They are effective in • subarachnoid hemorrhage (as they decrease vasospasm), and
• hemorrhagic and ischemic strokes.

They should be used within the first 12 hours after the insult.

Mechanism: • Cerebral vasodilation resulting in increased CBF.
• Reduction of Ca^{++} entry resulting in decreased cellular injury.
• Modulation of free fatty acid metabolism.

2- Na Channel Blockers: (Lamotrigine and Lidocaine).

Lamotrigine is an anticonvulsant while lidocaine is a local anesthetic agent.

They are effective in global and focal ischemia such as subdural hematoma, head trauma and middle cerebral artery occlusion.

3- Methylprednisolone:

Dose: 30 mg/kg bolus then 5.4 mg/kg/day for 2 days given within 8 hours from the insult.

It is effective in spinal cord injury.

Mechanism: see before.

4- "21"-Aminosteroids: (Tirilizad).

It has doubtful results in subarachnoid hemorrhage.

Mechanisms: It acts as a potent inhibitor of O_2 free radical induced lipid peroxidation.

5- N-Methyl D-Aspartate (NMDA) Receptor Antagonists: They are either:

a- Noncompetitive:

1- **Remacemide**: It decreases the incidence of strokes in patients undergoing coronary artery bypass grafting surgery.

2- **Magnesium (Mg^{++})**: It is used in acute ischemic stroke patients and traumatic brain injury by **Field Administration of Stroke Treatment-Magnesium (FAST-MAG)** where it is used soon after trauma in a dose of 4 g i.v. It gives good results and improves neurologic recovery.

3- **Xenon**: It has some neuro-protective action.

4- **Ketamine** is discussed above.

5- Others:
- Dextromethorphan.
- Dextrophan anti-tussives.
- Dexmedetomidine.
- MK-801
- Aptiganol.
- N_2O.

NMDA antagonists decrease the release of glutamine (excitatory neurotransmitter), so they prevent neuronal damage from excessive glutamine, but they also decrease GABA release (inhibitory neurotransmitter); therefore, **general dis-inhibition** occurs resulting in more neuronal damage and high side effects as hallucinations.

b- Competitive:

Selfotel is also not used due to its high side effects.

6- Adenosine Modulating Agents: (Acadesine).

It is effective in decreasing strokes in patients undergoing coronary artery bypass grafting surgery.

7- Free Radical Scavengers:

a- Hydroxyl-Scavenger: (Nicaravan).

It is effective in aneurysmal subarachnoid hemorrhage.

b- PEG-SOD (Pegorgotein):

Superoxide dismutase (SOD) is a physiologic free radical scavenger. It decreases cellular oxidative stress. It is present in 2 forms:
- Cytosolic copper-zinc SOD.
- Mitochondrial manganese SOD.

SOD can not cross blood brain barrier and cellular membranes; therefore, SOD is conjugated with polyethylene-glycol (PEG) to increase its penetration power.

Future Concepts in Brain Protection

1- Nitric Oxide (NO):

"nNOS" and "iNOS" are harmful while "eNOS" is beneficial during brain ischemia and infarction (see above); therefore, **designing drugs that selectively inhibit nNOS and iNOS while stimulating eNOS will decrease ischemic effects on neuronal tissues.**

2- Polymorpho-Nuclear Leukocytes:

ICAM and VCAM play a great role during ischemia and inflammation (see before); therefore, **designing drugs that inhibit VCAM and ICAM will decrease the infarction size after focal ischemia and reperfusion.**

3- Apoptosis (Programmed Cell Death):

Interleukin converting enzyme-like proteins (ICE-like protein) such as calpain and caspases have a great role during apoptosis; therefore, **designing new drugs that can inhibit ICE-like proteins will be used to protect the brain such as:**
- ICE inhibitors as z-VAK. FMK.
- Protein synthetase inhibitors as cycloheximide.

4- Cerebral Preconditioning:

Cerebral preconditioning is induction of controlled conditions that subject the brain to stress and allowing the brain to produce **endogenous proteins of repair e.g., erythropoietin (EPO)** that protect the brain later on when it is subjected to periods of ischemia or hypoxia.

Recent research shows the following **evidence**:
- Inducing cerebral preconditioning 18-24 hours before elective neurosurgery is beneficial.
- The neurons of rats subjected to heat shock (15 min at 41 °C) are protected from high intensity light damage if the rats have been allowed to recover for 18 hours following the heat exposure.

- Transient ischemic attacks induce ischemic preconditioning in humans.

Clinically acceptable methods of induction of preconditioning are still under research. Experimental results suggest that preconditioning can be induced by:

- **Preoperative hyperbaric oxygen therapy.**
- **Electro-convulsive therapy.**
- **Potassium channel openers as diazoxide.**
- **Erythropoietin (EPO):**

  It is **the most promising**. It is an endogenous substance produced in the brain after hypoxic or ischemic insult. It is a cytokine growth hormone that increases production of erythrocytes by preventing their apoptotic self-destruction during differentiation besides its effects on the brain.

  It is produced in the brain **by astrocytes** in the ischemic penumbra where it binds to **EPO receptors** which are up-regulated during ischemic penumbra causing the following events:

  - An increase in proteins of repair.
  - A decrease in neuronal excitotoxicity and inflammation.
  - Inhibition of neuronal apoptosis.
  - Stimulation of both neurogenesis and angiogenesis.
  - A decrease in the infarct size.

  It is administered by i.v. injection of recombinant EPO once daily for 3 days. This increases EPO in the central nervous system by 60-100 folds.

5- Hemi-Craniectomy:

Some surgeons do hemi-craniectomy after middle cerebral artery stroke to decrease the mortality by about 60%, but the results are doubtful.

Anesthesia for Craniotomy (For intracranial masses)

Causes of Intracranial Mass

1- Congenital.
2- Tumor (benign or malignant).
3- Infection (abscess or cyst).
4- Vascular (hematoma or malformation).

Clinical Picture:

A) If a Slowly Growing Mass, the patient is asymptomatic for a long period then finally symptoms occur.

B) If a Rapidly Growing Mass, the patient will suffer from:

1- General decline in cognitive or specific neurological functions.
2- Focal neurological deficits.

a- **Supra-tentorial masses** cause seizures, hemiplegia, aphasia and increased ICP.

b- **Infra-tentorial masses** i.e., masses in the **posterior fossa** (containing the medulla, pons, and cerebellum) may cause:

- Cerebellar dysfunction as ataxia, nystagmus, and dysarthria.
- Obstructive hydrocephalus which results in increased ICP due to obstruction of CSF flow at the level of the 4th ventricle or the cerebral aqueduct.
- Brainstem compression resulting in
  - cranial nerve palsies,
  - altered consciousness, and
  - vital center affection such as:
    - abnormal respiration or
    - abrupt changes in blood pressure and heart rate.

3- Increased ICP symptoms such as headache, effortless vomiting ± nausea, papilloedema, unilateral pupillary dilatation, altered consciousness and finally coma and brain herniation.

N.B.: Infra-tentorial craniotomy = posterior fossa craniotomy = sitting craniotomy = cerebello-pontine angle craniotomy.

Treatment of Intracranial Tumors:

1- Surgical resection or debulking.
2- Chemotherapy.

3- Irradiation either traditional irradiation or gamma knife irradiation. The latter differs from traditional irradiation in that multiple radiation sources are used and by addressing the tumor from multiple angles (by magnetic resonant imaging to obtain a 3 dimension image), radiation to the tumor can be maximized while radiation dose to any single area of surrounding brain can be diminished. The same approach can be accomplished with the use of radiation produced by a linear accelerator.

Preoperative Management:

Preoperative Evaluation:

1- Neurological Assessment: should be documented for:

- Clinical picture of the lesion as discussed above.
- Mental status by Glasgow coma scale.
- Sensory or motor deficits.
- Presence of muscle wasting (for hyperkalemia).
- Intracranial hypertension by assessing ICP.

2- Presence of Coexisting Diseases: for examples, hypertension, diabetes mellitus, ischemic heart diseases…etc and their management.

3- Drug Therapy: for precautions and side effects.

Especially:
- Corticosteroids as they can cause induced hyperglycemia.
- Diuretics as they can cause electrolyte imbalance.
- Anticonvulsant serum levels should be checked.

4- Preoperative Investigations:

Critically ill patients should be closely monitored during the investigations.

Restless or uncooperative patients may need general anesthesia.

Routine investigations are performed in addition to:

- CT and MRI for assessment of the brain tumor and edema (figure 15-16 and figure 15-17).
- ICP measurement if intracranial hypertension is suspected as discussed above.
- Chest x-ray to exclude secondaries in case of malignant tumors.

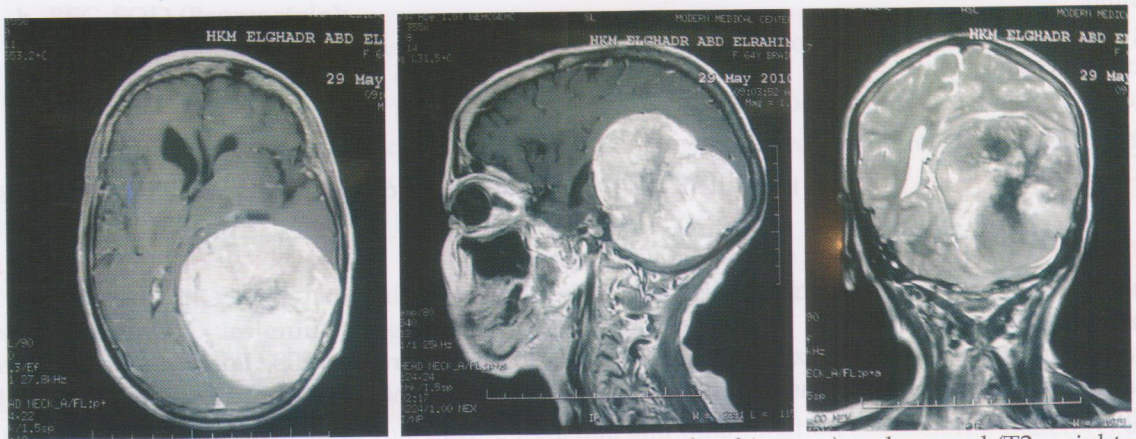


Figure 15-16: MRI axial and sagittal (post-contrast T1 weighted images) and coronal (T2 weighted image) of the brain (from left to right) showing a patient with a large cerebral tumor

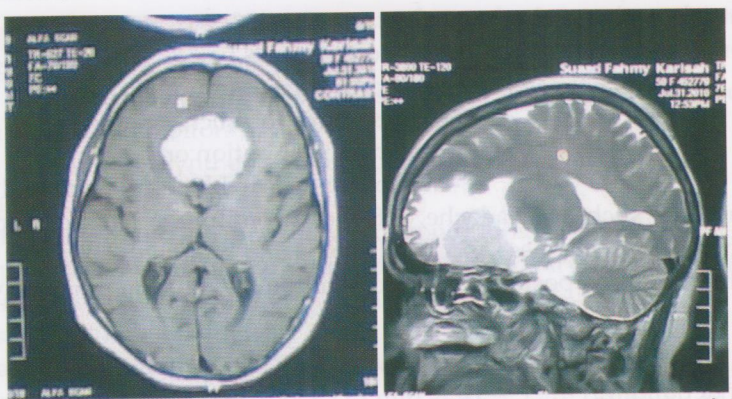


Figure 15-17: MRI axial T1 weighted image and sagittal T2 weighted image of the brain showing a brain tumor surrounded by localized brain edema which appears white on T2

Preoperative Patient Preparation:

1- Measures to decrease ICP: can be started preoperatively if ICP is high such as:

- Fluid restriction.
- Decreasing cerebral venous pressure e.g., head up tilt.
- Cerebral dehydrating measures e.g., mannitol and diuretics.
- Drugs that increase cerebro-vascular resistance e.g., thiopentone and lidocaine.
- Steroids: dexamethasone for brain tumors or abscess (not used in head trauma).
- Decreasing CSF volume as ventriculostomy just before induction.

More details are discussed above.

2- Measures to decrease venous thrombo-embolism due to lengthy operations.

The prophylactic and active management are discussed in the chapter of "Respiratory Disease".

3- Medications such as steroids, anticonvulsants, antihypertensive drugs and anti-anginal drugs should be continued till time of surgery.

Premedications:

1- Sedatives such as oral diazepam or i.m. midazolam.

- Conscious patients with normal ICP should receive small doses to prevent anxiety which can cause hemodynamic instability.
- Patients with increased ICP and altered conscious level should not receive any sedatives as they may cause hypoventilation and hypercarbia which in turn increases CBF and increases ICP further.

2- Prophylactic antibiotics may be given.

Intraoperative Management:

Aim: To maintain adequate cerebral perfusion.

Monitoring:

1- ECG: It is one of the standard monitors. It is important to detect dysrhythmias that may occur during surgical retraction or manipulation of the brainstem or cranial nerves or that occur with air embolism if occurs.

2- Pulse Oximetry: It is one of the standard monitors. It is important to detect hypoxia during air embolism.

3- Noninvasive Blood Pressure: It is one of the standard monitors. It is important to detect hypotension that may occur with air embolism.

4- Capnography: It is one of the standard monitors. It is important to facilitate $PaCO_2$ management and to detect hypocapnia that may occur with air embolism.

5- Urine Output: It is important during:

- the frequent use of diuretics,
- the long duration of surgery,
- guidance of fluid therapy, and
- cerebral salt losing syndrome (see later).

6- Body Temperature (Nasopharyngeal or Esophageal): It is important due to the following:

- The long duration of surgery.
- If hypothermia is used to decrease ICP or to detect and prevent hypothermia if present.

7- Invasive Blood Pressure Monitoring: to ensure optimum cerebral perfusion.

Many neuro-anesthesiologists zero the arterial pressure transducer at the level of the head (external auditory meatus) instead of the right atrium to facilitate calculation of cerebral perfusion pressure.

8- Arterial Blood Gas Analysis: is important to regulate $PaCO_2$ and enable proper control of ICP ($ETCO_2$ alone is not enough).

9- Central Venous Pressure Monitoring: is important for:

- Patients receiving vasoactive drugs.
- Judging fluid therapy and volume status.
- Aspiration of venous air embolism if it occurs (with the tip of the catheter in the right atrium).

Some avoid the use of the internal jugular vein for catheterization and use antecubital, subclavian, or external jugular vein instead for catheterization because:

- There is a risk of carotid puncture with internal jugular catheterization.
- It may interfere with venous drainage from the brain.

10- Pulmonary Artery Catheterization: is important for:

- assessing fluid therapy and volume status.
- monitoring of cardiac output in patients who have had preoperative cardiac problems.

Care must be taken to use minimal head-down necessary to access the central venous circulation because severe trendelenburg position has a deleterious effect on ICP and CPP.

11- Neuromuscular Monitoring: is important for:

- avoiding intraoperative straining and coughing.

It is done on the non-affected side in patients with hemiparesis because the paresis makes the twitch response resistant and suppressed due to proliferation of acetylcholine nicotinic receptors that occur after denervation.

12- Cerebral Function Monitoring (it is not a standard monitor in most hospitals)

a) Electroencephalography (EEG):

- Although it has been used to monitor cerebral ischemia, scalp electrodes may not reflect the activity of brain areas mostly at risk.
- Cortical electrodes are preferred to scalp electrodes as they may avoid the problem of attenuation of the scalp EEG signals by CSF drainage and air between the scalp electrodes and the brain surface during surgery.

b) Evoked Potentials:

- Somatosensory Evoked Potentials (SSEPs): Although they may detect reversible cerebral ischemia during temporary vessel occlusion, they may not detect ischemia in sub-cortical structures and motor cortex. Also they have high false positive and false negative results.
- Visual Evoked Potentials: to prevent optic nerve damage during resection of pituitary tumors.
- Brainstem Auditory Evoked Potentials (BAEPs): to prevent the 8th cranial nerve injury during **posterior fossa craniotomy** e.g., acoustic neuroma or aneurysm.

13- Electromyography:

- To prevent injury of the facial nerve in **posterior fossa craniotomy**. It needs incomplete muscle paralysis.

14- ICP Monitoring: Although it is **not routinely** done, it is the most accurate and reliable method for ICP monitoring. It is performed in cases with increased ICP by a small catheter inserted by the neurosurgeon under local anesthesia either into the lateral ventricle (ventriculostomy), over the cerebral cortex, in the subdural space, or in the epidural lumbar space (the most common).

Ventriculostomy also is used to withdraw some CSF to decrease ICP. ICP monitoring is discussed in more details in chapter "Monitoring during Anesthesia & Intensive Care".

15- Special Monitors for Venous Air Embolism: (in posterior fossa craniotomy)

- Precordial or esophageal stethoscope.
- Precordial Doppler ultrasound probe.
- Trans-esophageal echocardiography.

In addition to the useful information obtained by these monitors, they are **very sensitive** to detect the **precordial Millwheel murmur** of venous air embolism.

16- Jugular Vein O_2 Saturation (SjO_2)

It is measured by a fiberoptic oxy-metric catheter placed in **the bulb of the jugular vein** which passes retrogradely under x-ray for continuous monitoring of cerebral O_2 extraction to assess global cerebral perfusion and CBF. More details are discussed in the chapter of "Monitoring during Anesthesia & Intensive Care".

Choice of Anesthesia:

A) Local Anesthesia (Awake Craniotomy):

Indications: (and advantages)

An awake craniotomy is mainly indicated in the following conditions:

1- Increased ICT with **slight operative intervention** e.g., burr hole biopsy.

2- **Functional neurosurgery:** when **the patient's cooperation is required** as localization of subjective phenomenon after cortical electrical stimulation such as:

- **speech monitoring,**
- **epilepsy surgery,**
- **surgeries for Parkinson's disease,** and
- **surgeries** to remove slowly growing or benign tumors from **areas near the main motor and sensory gyri** to allow maximal tumor resection without affection of the motor or sensory areas.

These surgeries require **mapping of the brain** to identify the area of the surgery itself from the areas of the brain to be left such as the motor area to decrease postoperative neurological deficits.

3- Increased ICP for some **emergency craniotomies** e.g., middle meningeal artery ligation.
4- **Very poor general condition of the patient** which contraindicates general anesthesia.

Disadvantages:

1- It is unsuitable for uncooperative patients.
2- It is unsuitable for some conscious patients due to the strain produced by the long duration of surgery.

Anesthetic Management:

Preoperative Management:

Besides all the preoperative management of ordinary craniotomies:

- The **anesthesiologist must explain** to the patient that he or she will be awake during a part if not all of the procedure and that this is required so that the healthy part of the brain can be identified and not injured. It is important to review with the patient what will be required from him or her such as the questions that may be asked to assess the speech center ,and the tasks required such as "move your toes".
- **Premedication**:
  - **Avoid sedatives** or **only give a minimal dose when full patient's cooperation is needed**. I.v. diazepam is given to decrease the risk of epilepsy if it is suspected.
  - **Clonidine** may be used as a premedication.
  - **Antiemetics** such as ondansetron or metoclopramide are to avoid intraoperative emesis because vomiting may injure the awake patient.

Intraoperative Management:

Besides all the intraoperative management of ordinary craniotomies:

a) If the Patient is Awake during the Whole Procedure:

- **Minimal doses of sedatives** are needed. Propofol, midazolam, remifentanil, or alfentanil are commonly used for sedation and analgesia.
- **Local infiltration** of skin and scalp with 2% lignocaine with adrenaline 1:100 000 is required.

N.B.: • Bone is slightly sensitive, but periosteum is very sensitive.
• Brain tissues (cranial contents) are insensitive except:
- Dura mater attached to the bone of the skull.
- Dura around middle meningeal artery.
- Nervous spinous tissues.
- Trigeminal ganglia.

b) If Wake up Test is required:

- General anesthesia is induced with laryngeal mask airway for craniotomy which is followed by intraoperative awakening for neurological assessment. After that, general anesthesia with laryngeal mask airway is induced again until completion of surgery. More details of wake up test are discussed in chapter "Monitoring during Anesthesia & Intensive Care".

Generally, anesthetics which are used should **not interfere with the EEG** or evoked potentials such as:

- **< 0.5 MAC of isoflurane** with 2-4 µg/kg fentanyl is a good choice.
- **Full muscle relaxation** is needed to avoid muscular artifacts, but it is **avoided if motor mapping** is planned.
- If the blood pressure rises due to a lighter plane of anesthesia, labetalol or esmolol is recommended (nitroprusside and hydralazine are not recommended as both may produce changes of cerebral blood flow because they increase heart rate).
- If the surgeon asks for more patient cooperation, reversal of medication may be needed e.g., flumazenil (for sedatives), naloxone (for narcotics), and even prostigmine with atropine (for reverse of muscle relaxants).
- If the patient complains of pain, small doses of remifentanil 0.01 to 0.05 mg/kg/min for 3-5 minutes combined with propofol 15 µg/kg/min are effective in conscious sedation.

Postoperative Management:

All the postoperative managements of the ordinary craniotomies are applied.

B) General Anesthesia: the most commonly used.

Induction:

- **Preoxygenation** with voluntary hyperventilation (in a cooperative patient) to decrease ICP is needed.

• **Smooth induction** to avoid further increase in ICP is a good choice. **The pressor (stress) response of intubation can be avoided** by:
  - deepening anesthesia by volatile agents especially isoflurane
  - i.v. opioids such as fentanyl 2-8 μg/kg
  - decreasing the laryngoscopic time
  - lidocaine: i.v., topical anesthesia of the airway, intra-tracheal, or spray, or
  - i.v. β-blockers.

The use of hypotensive agents as nitroprusside or nitroglycerin should be avoided as they both cause cerebral vasodilation which further increases CBF and ICP.

Rapid sequence crush induction is done if there is a **risk of aspiration**. Some anesthesiologists consider patients with **increased ICP** to have an increased risk of aspiration due to the presence of vomiting; therefore, crush induction is commonly indicated in these patients.

• **Induction agents:** Avoid drugs which increase CBF and in ICP.
  - **Thiopentone** provides greater **brain protection** as it decreases CBF and ICP.
  - **Propofol** decreases CBF and ICP and also **allows early recovery**.
  - **Etomidate** decreases CBF and ICP, but recently some claim that the standard propylene glycol which is used in formulation of etomidate induces cerebral hypoxia and tissue acidosis and so it is better **avoided**.
  - **Ketamine** should be **avoided** because it increases CBF and ICP.
  - **Inhalational induction in children** should be **avoided** because it increases CBF and ICP and makes the child distressed which further increases in ICP.

• **Muscle relaxants:**
  - Nondepolarizing muscle relaxants such as rocuronium, vecuronium, pipecuronium, cis-atracurium, or doxacurium can be used because:

    They have no effect on CBF and ICP. The **nerve stimulator** should be used to ensure adequate muscle paralysis to avoid coughing with intubation.

    They also have no effect on hemodynamic status.
  - Succinylcholine is used especially if there is suspected difficult intubation or potentially full stomach. It should be used with the following precautions:
    - It may increase ICP due to fasciculations; so, a defasciculating dose of nondepolarizing muscle relaxants may be given.
    - It may produce severe hyperkalemia in patients with significant muscle wasting and paralysis.

• **The endotracheal tube** should be **armored** latex (non-kinkable) tube, and should be **well secured**, and **re-checked after positioning**.

Position:

a- Supine position is indicated for frontal, temporal, and parieto-occipital craniotomies. The following precautions should be taken:
  - The head is usually elevated **15-30 degrees** to facilitate venous and CSF drainage.
  - The head may be turned to the side to facilitate exposure, but **excessive twisting** of the neck should be avoided as this may cause jugular venous drainage obstruction resulting in increased ICP or arterial compression in the elderly resulting in vertebro-basilar insufficiency.

b- Modified lateral position (three-quarter prone-park bench position or semi-prone position): The patient is turned toward a more prone position, moving the upper shoulder out of the surgeon's view.

c- Prone position.

d- Sitting position.

The last 3 positions are usually indicated in **posterior fossa craniotomy**.

Sitting Position:

It is preferred by most surgeons (but not by anesthesiologists) because:
  - It allows better access to the tumor especially large or midline tumors.
  - It increases venous and CSF drainage.

Technique:

A patient is actually semi-recumbent in the standard sitting position as the back is elevated to 60 degrees while the legs are elevated with the knees flexed to the level of the heart to prevent venous pooling and decrease the risk of venous thrombo-embolism. The head is fixed in a three-point holder called **(May field holder)** with the neck flexed while the arms remain at the sides with the hands resting on the lap (figure 15-18).

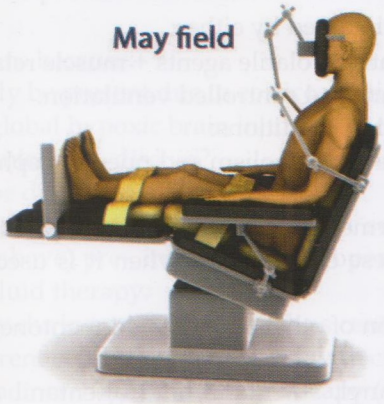


Figure 15-18: Sitting position

Contraindications of Sitting Position:

a- Absolute:
- Intra-cardiac defects.
- Pulmonary arterio-venous malformation.
- Right atrial pressure > left atrial pressure.
- Patent foramen ovale.
- Cerebral ischemia when upright and awake.

b- Relative:
- Severe hypovolemia or uncontrolled hypertension.
- Extremes of age.
- Severe cachexia.
- Severe hydrocephalus.
- High lesion vascularity.
- Chronic obstructive pulmonary disease.

Complications and Precautions of Sitting Position:

1. **Postural Hypotension:** due to
   - pooling of the blood into the lower extremities,
   - the intentional volume depletion induced by fluid restriction and diuresis, and
   - blunting or abolishing of the compensatory sympathetic reflexes by general anesthesia.

Therefore, the following precautions should be taken:
- **Gradual** positioning with **blood pressure monitoring** is essential.
- **Wrapping the legs with elastic bandages or stockings** (from the feet to the upper thigh) before positioning to decrease venous pooling and decrease incidence of deep venous thrombosis.
- Using **light anesthesia during positioning** helps in maintaining sympathetic tone.
- **Small doses of a vasopressor** as ephedrine or phenylephrine may be used (they are preferred to i.v. infusion of large amounts of fluids).

2. **Hypertension** may occur due to the pins of the head-holder; therefore, it is better to infiltrate local anesthetics at the sites of the pins.
3. **Avoid injury of pressure points** such as elbow, ischial spines, or forehead by protecting them by foam padding.
4. **Avoid excessive neck flexion** because:
   - It impedes venous drainage resulting in an increase in the ICP and causes swelling of the upper airway.
   - Rarely, it may cause compression of cervical spinal cord, especially if the patient has preexisting cervical spinal stenosis that may result in quadriplegia.
5. **Increased incidence of venous air embolism or pneumocephalus**.

Generally, during any positioning:
- The endotracheal tube and i.v. cannula should be well secured. All the breathing circuit connections and i.v. lines should be checked as both the patient and the connections are almost completely covered by surgical drapes.
- Recheck the proper position of the tube after positioning.
- The eyes of the patient should be covered.

• Shaving of the head is usually done after induction and before positioning.

Maintenance: Craniotomy can be maintained by either:

• $O_2 \pm N_2O$ + opioids + low concentration volatile agents + muscle relaxants and controlled ventilation.

or • Total i.v. anesthesia + muscle relaxant and controlled ventilation.

N_2O: should be **avoided** with the following conditions:

• Sitting position as it increases venous air embolism and pneumocephalus.

• Intracranial cyst.

• Air encephalography (it is not performed nowadays after the advance of CT and MRI).

N_2O increases CBF, ICP, and CMR. These effects occur when it is used alone, but in combination with other agents variable effects occur.

N_2O decreases the neuro-protective action of other agents as thiopentone or isoflurane.

Opioids:

• Short acting opioids such as fentanyl, sufentanil, and alfentanil are used to avoid postoperative respiratory depression.

• They have little or no effects on CBF and ICP. Fentanyl may decrease ICP; therefore, it may be preferred.

Low Concentration Volatile Agents: can be used, but large doses should be avoided because all volatile agents increase CBF and ICP especially before opening the dura. They are used if there is no risk of increased ICP.

• **Isoflurane** is of **choice** because it has the least effects on CBF and ICP.

Total intravenous anesthesia (TIVA): (Propofol + alfentanil infusions):

• TIVA is used if there is a risk of increased ICP. It is **preferred by some authors** because:

1- It allows **rapid postoperative recovery** and thus, rapid assessment.

2- It allows **intraoperative awakening** of patients to move in response to command for neurological assessment e.g., during spinal surgery or trigeminal nerve surgery.

3- **It decreases the incidence** of postoperative **shivering** and postoperative **nausea and vomiting.**

Muscle Relaxants: as in induction.

Controlled Ventilation:

• **Moderate hyperventilation** is needed to maintain $PaCO_2$ between **35-40 mm Hg** (30 mm Hg in selected in some cases for short periods) to decrease ICP.

• Avoid severe hypocapnia as it causes cerebral vasoconstriction which increases cerebral ischemia.

• Avoid hypercapnia as it causes cerebral vasodilation resulting in increased CBF and ICP and may cause steal phenomenon in focal cerebral ischemia which increases intracellular acidosis.

• Avoid positive end-expiratory pressure (PEEP) and high airway pressures because both increase central venous pressure which in turn increases ICP.

Intraoperative Fluid Management:

Amount:

Intraoperative fluids should be **moderately restricted** (i.e., below the calculated amount) especially in patients with severe brain edema or increased ICP because:

• This allows greater osmotic effects of mannitol in a smaller circulation volume.

• Mannitol causes circulatory overload; so, if the blood volume is large, it may increase the risk of pulmonary edema.

• It facilitates induced hypotension in vascular lesions.

• It decreases the risk of postoperative edema.

Types:

• Isotonic crystalloids e.g., normal saline or ringer solution is used for maintenance (avoid hypotonic solutions e.g., lactated ringer, 0.45% sodium chloride, or dextrose 5% solution because they decrease the plasma osmolality).

• Colloid solutions e.g., human albumin or hydroxyl ethyl starch solution is used to restore intravascular volume deficits (if only crystalloids are given they may cause dilutional effects i.e., they may decrease the colloidal osmotic pressure of plasma resulting in increasing in the brain edema; therefore, colloids should be used with crystalloids).

• Hypertonic solutions e.g., mannitol, urea, or hypertonic saline.

• Blood transfusion: Usually packed red blood cells are used. Care should be taken as occult blood loss may occur underneath the surgical drapes or on the floor.

Precautions:
Avoid hypotonic solutions.
Avoid glucose containing solutions because:
- Hyperglycemia may already be present due to corticosteroids.
- Hyperglycemia increases global hypoxic brain injury by increasing cerebral acidosis.

Q: Fluid management during craniotomy, discuss?
A: The following points should be discussed:
- Introduction about osmolarity, hypertonic and hypotonic solutions.
- Amount of fluid given (as above) pre-, intra-, and post-operatively.
- Types and precautions of fluid therapy.
- Monitoring of fluid therapy during craniotomy such as central venous pressure and urine output.
- Fluid management in different conditions associated with craniotomy such as diabetes insipidus, head trauma, subarachnoid hemorrhage, and HHH therapy (see later).

Intraoperative Complications and Problems:

1) Brain Protection Methods:

Continue the preoperative measures as above such as:
1- Keep normal O_2 carrying capacity by keeping hematocrit (Hct) between 30–40% and keeping normal PaO_2.
2- Keep normal blood glucose between 100-150 mg/dL. It should be measured every 2 hours.
3- Maintain mild hypothermia (33-36°C).
4- Administer thiopentone infusion.
5- Administer mannitol infusion.
More details are discussed above.

2) Measures of Reduction of Intracranial Hypertension:

Continue the preoperative measures as above such as fluid restriction. These measures are discussed above.

3) Intraoperative Hypertension:

Causes:
- Surgical stimulation.
- Increased ICP which is associated with bradycardia (Cushing reflex).

Treatment:
- At first, **deepen the anesthesia** by sub-MAC doses of isoflurane or additional doses of thiopentone.
- **β-blockers** such as esmolol or labetalol are given (they also decrease heart rate).
- **Avoid vasodilators** such as nitroprusside, nitroglycerin, Ca^{++} channel blockers, or hydralazine especially before opening the dura as they produce cerebral vasodilation which in turn increases CBF and ICP.

4) Intraoperative Hypotension:

Causes:
- Hypovolemia or blood loss; therefore, they should be assessed and managed.
- Vasodilation.

Treatment: vasopressors such as ephedrine or phenylephrine. Both are preferred than i.v. fluids.

5) Intraoperative Bradycardia:

Causes:
- **Cushing reflex**: Elevated ICP increases the blood pressure and decreases heart rate.
- **Vagal reflex** due to
  - Stimulation of cranial nerve roots.
  - Vascular surgery around circle of Willis and internal carotid artery.

Treatment: immediate anticholinergic drugs e.g., atropine.

6) Intraoperative Hypothermia:

Cause: The long duration of operation.
Treatment: heated blankets, warm i.v. fluids…etc.

7) Special Problems of Posterior Fossa Craniotomies:

a- Obstructive Hydrocephalus:

It may cause marked increased in ICP; therefore, a ventriculostomy is often performed under local anesthesia to decrease ICP prior to induction of general anesthesia.

b- Brainstem Injury:

1. **Injury of vital centers** due to direct surgical injury, retractor pressure, intraoperative ischemia or edema.

Respiratory center injury causes postoperative inability to maintain patent airway as well as irregular respiration; therefore, spontaneous ventilation may be used by some anesthesiologists to detect intra-operative respiratory injuries.

Cardiovascular center injury causes changes in blood pressure, heart rate, and rhythm.

2. **Injury of cranial nerves:**

5th, 7th, and 8th cranial nerve injury causes loss of corneal reflexes, lid closure, and hearing defects.

10th cranial nerve injury causes impaired swallowing, aspiration and difficulty to maintain a patent airway.

c) Pneumocephalus:

It is entry of air to the **subarachnoid space** during surgery especially occurring with the sitting position. Using **N_2O** causes **expansion** of pneumocephalus after dura closure. This compresses the brain resulting in delaying or preventing awakening after anesthesia; therefore, N_2O should be discontinued before the dura is closed. Some authors do not prefer using N_2O at all in sitting craniotomies.

d) Venous Air Embolism:

The incidence in posterior fossa craniotomy is 20–40%. Pathology, clinical picture, monitoring, and management are discussed in details in the chapter of "Respiratory Disease".

Emergence:

The patients are either:

a) Left intubated with muscle relaxation, mechanical ventilation and sedation.

These are patients with severely increased ICP and brain edema.

b) Extubated at the end of the surgery **in operating room** or **within 1-2 hours i.e., Fast-Track Neuro-Anesthesia**

Indications: Patients without increased ICP.

Advantages:

1- It allows **early clinical monitoring** of the patient and **early treatment of postoperative complications.**

2- It avoids **the complications of prolonged sedation and mechanical ventilation** as pneumonia, baro-trauma, and pneumothorax.

3- It decreases the time of the intensive care unit stay and the cost of treatment.

Contraindications:

1- Increased ICT e.g., • Pre-existing decreased level of consciousness.
- Severe traumatic brain injury.
- Large brain tumors with extended zone of edema.
- Extended IC bleeding.
- Significant vasospasm after IC vascular surgery.
- Significant intraoperative brain swelling.

2- Craniotomy for infra-tentorial lesions close to the brainstem or sitting craniotomy.

3- Poor general condition (ASA > III).

Technique:

• **Smooth Extubation:**

Suction is done while the patient is deeply sedated to avoid coughing, straining or bucking on the endotracheal tube because this may cause intracerebral hemorrhage, worsening of brain edema and increase of ICP.

Smooth extubation is performed by one or combination of the following methods before suctioning to suppress coughing:

- Lidocaine 1.5-2 mg/kg i.v. or filling the cuff of the endotracheal tube especially with alkalinized lidocaine.
- Small doses of propofol 20-30 mg.
- Small doses of thiopentone 25-50 mg.
- Ca^{++} channel blockers such as verapamil (0.1 mg/kg i.v.) or diltiazem (0.2 mg/kg i.v).
- β-blockers such as esmolol infusion 200 µg/kg/min.
- α_2-agonists such as clonidine (3 µg/kg i.v. preoperatively) or dexmedetomidine (2 µg/kg i.v.).

• After application of head dressing and full access to the patient is regained, (i.e., the table is turned back to its original position at induction) extubation is done.

Complications:

1- Postoperative hypoventilation resulting in hypoxia and hypercarbia due to residual action of long acting opioids and other sedatives. This causes severely increased ICP and brain edema.

2- Hemodynamic changes due to stress, pain, and/or coughing on awakening.

Postoperative Management and Intensive Care Considerations:

The patient is usually transferred to an **intensive care unit**.

1) Close monitoring of • **neurological** function (early assessment),
• **cardiovascular** function such as ECG and blood pressure.
• **respiratory** function as respiratory depression due to residual effect of anesthetic drugs causes hypercarbia and hypoxia which further increase the ICP.
• **ICP** and its management if still high.

2) Postoperative Care:
- Patients generally have minimal pain but **postoperative analgesia** is essential.
- Patients should be in **semi-sitting position**.
- Continue **moderate fluid restriction and avoid glucose** containing solutions.

3) Postoperative Complications:

1- **Elective postoperative ventilation** is done in patients with a severe increase in ICP and brain edema with muscle relaxants and sedation.
2- **Anticonvulsant therapy** to control seizures e.g., diazepam or phenytoin.
3- Postoperative **shivering**.
4- Psychomotor disturbances.
5- Nausea and vomiting.
6- Intracerebral hematoma.
7- Laryngeal swelling due to long standing procedures and intubation with extreme head flexion.

Anesthesia for Intracranial Aneurysm

Incidence:

5% of general population.

Site of Intracranial Aneurysm:

Intracranial aneurysm occurs in the branches of **circle of Willis** (discussed above).

1- Anterior circulation 39% is the most common site for intracranial aneurysm especially at the junction of the anterior communicating and the anterior cerebral arteries.
2- Internal carotid artery 30%.
3- Middle cerebral artery 22%.
4- Posterior circulation 8%.

Since the cerebral arteries course within the subarachnoid space, **rupture** of these arteries **typically** produces **subarachnoid hemorrhage**. However, intra-parenchymal and inter-ventricular bleeding may occur depending on the location of the aneurysm and the extent of bleeding.

N.B.: Cerebral Vascular Surgeries include:
1- Intracerebral aneurysm.
2- Arterio-venous malformation.
3- Carotid endarterectomy.
4- Moyamoya disease.

N.B.: Non-traumatic Intracranial Hemorrhage includes:
1- Ruptured aneurysm.
2- Ruptured arterio-venous malformation (AVM).
Both 1 and 2 are usually treated surgically.
3- Hypertensive crisis.
4- Spontaneous lobar hemorrhage.
Both 3 and 4 are usually treated medically.

Subarachnoid Hemorrhage

Causes:

Subarachnoid hemorrhage occurs due to rupture of: • **Cerebral aneurysm**: 75-80%.
• **Arterio-venous malformation (AVM)**: 4-5%.

Other causes: • Trauma. • Cocaine abuse. • Sickle cell disease.
• Mycotic aneurysm. • Coagulopathy.

Pathology:

Aneurysmal **rupture** causes **leakage** of the arterial blood in the subarachnoid space (and less commonly in the epidural space and brain). This causes **a rapid increase in ICP** which in turn decreases **cerebral perfusion pressure and CBF** leading to loss of consciousness. The fall in CBF decreases **the bleeding and stops the subarachnoid hemorrhage.** Then there is either:

- A gradual decrease in ICP and increase in CBF which indicate improved cerebral function and possibly regained consciousness.
- A persistent increase in ICP which indicates no flow pattern with acute vasospasm, cell swelling, and death.

Risk factors for rupture of cerebral aneurysm:

- Female sex.
- Use of oral contraceptives.
- Pregnancy.
- Vascular abnormalities (type III collagen deficiency and elastase abnormalities).
- Coarctation of the aorta.

- Hypertension.
- Smoking and alcohol abuse: They predispose to aneurysm formation and rupture.
- Cocaine abuse: It increases ICP and predisposes to aneurysm rupture.
- Polycystic kidney disease.
- Occurrence of cerebral aneurysms in the first-degree relatives.

Clinical Picture:

1) Increased ICP: It causes **headache** in 85-95% of patients.

- In unruptured aneurysm due to progressive enlargement.
- In ruptured aneurysm: ▫ Minor bleeding causes mild headache.
  ▫ Severe bleeding causes sudden severe headache (it is usually described as **the worst headache of the patient's life).**

2) Decreased CBF: It causes:

- **Loss of consciousness** for a brief period followed by return of consciousness.
- **Focal neurological lesions** which are sensory and motor deficits, cranial nerve palsies, and visual disturbances.

3) Blood in Subarachnoid Space: It causes:

- **Meningeal irritation** which produces nausea, vomiting, photophobia and nuchal rigidity (symptoms similar to infectious meningitis).
- **Fever** due to increased metabolic rate (as with head trauma).

4) Cardiovascular Effects of Subarachnoid Hemorrhage:

Pathology: Subarachnoid hemorrhage causes **injury of the posterior hypothalamus** which causes release of **norepinephrine** from the adrenal medulla and **cardiac sympathetic efferents**. This increases the afterload and causes direct myocardial toxicity which in turn causes **subendocardial ischemia** (pathological analysis of the myocardium of patients who have died acutely from subarachnoid hemorrhage shows microscopic subendocardial hemorrhage and myocytolysis).

Effects:

a- **ECG Changes:** occur in 50-80% of patients with subarachnoid hemorrhage.

- ST segment depression and T wave inversion are the most common and are scattered and not related to a particular distribution.
- Prolonged QT interval.
- Prominent U wave.
- Dysrhythmias in 80% of patients especially in the first 48 hours such as:
  ▫ Premature ventricular contractions (PVCs): the most common abnormalities.
  ▫ Torsade de pointes.
  ▫ Ventricular fibrillation or any other arrhythmias can occur.

Dysrhythmias are due to: increased catecholamine secretion,
increased cortisol secretion, and
hypokalemia.

b- **Ventricular Dysfunction:** in 30% of patients causing pulmonary edema. The apical cardiac function may be preserved; a phenomenon attributed to the paucity of sympathetic innervation at the cardiac apex.

5) Delayed Complications:

a- Cerebral Vasospasm: It occurs in 30% of patients. It occurs usually after 4-12 days post-bleeding pre- and mostly postoperatively (its management is discussed later).

b- Re-rupture: It occurs in 20% of patients during the first 2 weeks after the initial stage if the aneurysm is untreated with the highest risk in the first 24 hours. It is associated with 60% mortality. Some authors recommend treatment by anti-fibrinolytic therapy (e.g., aminocaproic acid) which may retard clot fibrinolysis and prevent re-bleeding, but this treatment may increase venous thrombo-embolism, cerebral vasospasm, and infarction.

c- Hydrocephalus: It is either:

- Acute which needs emergency ventricular draining or
- Chronic which needs delayed ventricular shunting.

6) Death may occur after rupture of the aneurysm in the subarachnoid space. It is either:

- Acute sudden death in 30% of patients, or
- Delayed death in 25% of patients.

Investigations:

1- Computerized Tomography (CT scan) (± contrast): is performed within 72 hours of symptoms to locate the site and the size of the aneurysm and bleeding.

2- Magnetic Resonant Imaging (MRI): is performed to locate the intra-parenchymal ischemic injury due to cerebral vasospasm (figure 15-19). It also can show the site of bleeding with FLAIR.

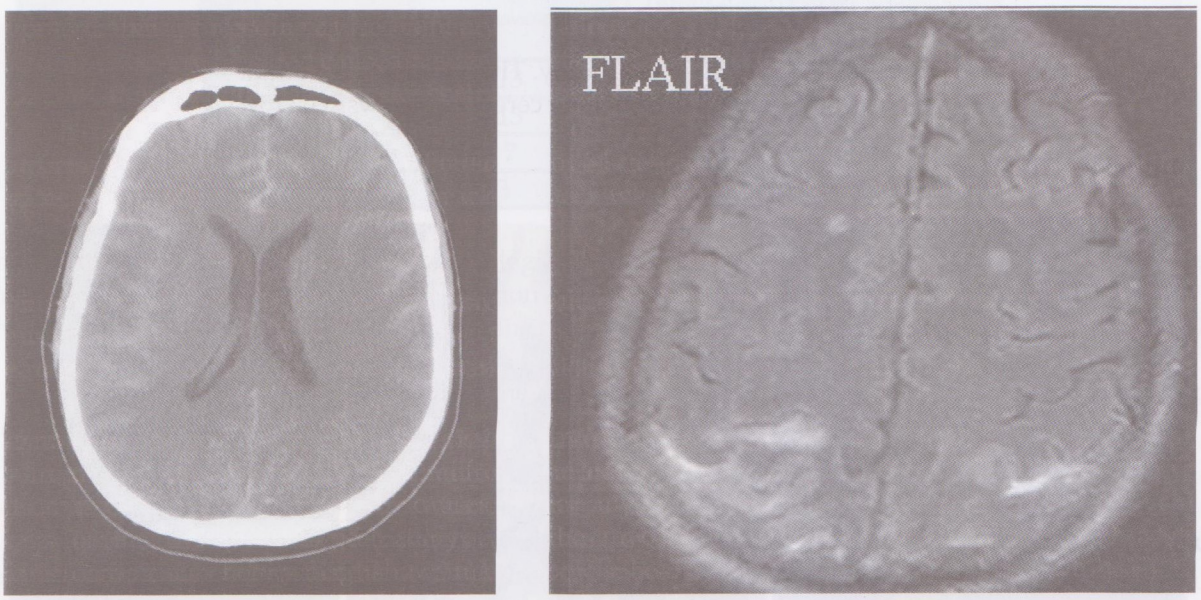


Figure 15-19: Subarachnoid hemorrhage; CT brain (the left image) with increased density in brain sulci denoting subarachnoid hemorrhage. MRI brain, FLAIR (fluid-attenuated inversion recovery) image (the right image) showing hyper-intensity in the parietal lobe.

3- Lumbar Puncture:

- It is important to diagnose subarachnoid hemorrhage if CT scan is negative especially in patients with suggestive history of rupture of an intracranial aneurysm.
- It can cause herniation or re-bleeding; so, for patients presenting within 72 hours of bleeding CT scan should be done instead.
- It shows
  - blood in CSF.
  - xanthochromia (yellowish discoloration of the CSF after centrifugation) which is present from 4 hours to 3 weeks after subarachnoid hemorrhage.
- CSF cultures must be sent to rule out meningitis.

4- Four vessel Angiography (right and left carotid and vertebral arteries) (figure 15-20): It is the gold standard investigation. It is used for:

- Visualization of all intracranial vessels.
- Localization of the source of bleeding.
- Ruling out multiple aneurysms.
- Diagnosis of cerebral vasospasm, which may require postponement of surgery.

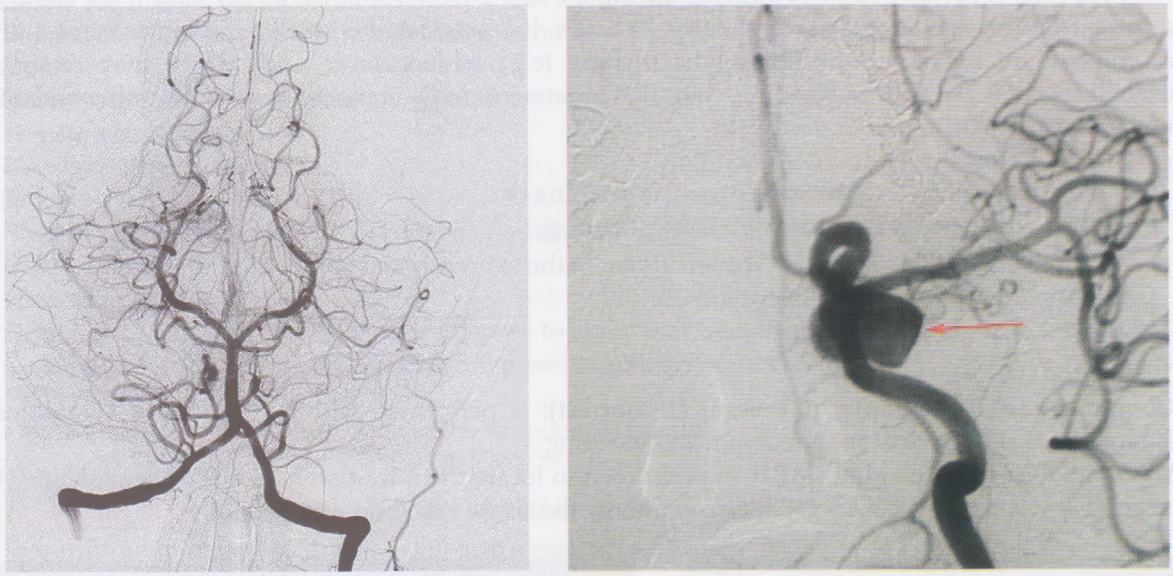


Figure 15-20: Cerebral angiography. The left image is normal while the right image shows a large cerebral aneurysm (arrow)

5- Multislice CT angiography (figure 15-21).



Figure 15-21: Multislice CT angiography of the cerebral vessels of a patient complaining of headache revealing a large oval shaped saccular aneurysm arising from the anterior communicating artery at the junction with the right anterior cerebral artery

6- Transcranial Doppler Ultrasonography:
It can be repeated serially at the bedside to diagnose cerebral vasospasm where there is increased cerebral blood flow velocity in spastic vessels.

7- ECG: shows cardiac dysrhythmias or ischemia.

8- Echocardiography: shows decreased contractility with pulmonary edema.

Assessment of Severity of Subarachnoid Hemorrhage

It is important to indicate the **prognosis** after subarachnoid hemorrhage and evaluate **the efficacy of therapy**.

A) Hunt and Hess Clinical Grading:

It is equivalent of the Glasgow coma scale in head trauma patients.

Grade	Criteria
0	Unruptured aneurysm (**asymptomatic**).
1	Ruptured aneurysm; asymptomatic or with **minimal headache** and slight nuchal rigidity, but no neurological deficit.
2	**Moderate to severe headache** with nuchal rigidity, but no neurologic deficit other than a cranial nerve palsy.
3	**Drowsiness**, confusion or **mild focal deficits**.
4	**Stupor, moderate to severe hemiparesis** and possible **early decerebrate rigidity and vegetative** disturbances.
5	**Deep coma, decerebrate rigidity and moribund appearance**.

Serious systemic disease such as hypertension, diabetes mellitus, severe vasospasm seen on arteriography, severe atherosclerosis, or chronic pulmonary disease puts the patient in the next worst grade.

B) World Federation of Neurologic Surgeons' Grade (WFNS Grades):

It is based on Glasgow coma scale.

Grade	Glasgow Coma Scale	Motor Deficit
0	15	Intact unruptured aneurysm
1	15	Absent ruptured aneurysm
2	14 – 13	Absent
3	14 – 13	Present
4	12 – 7	Absent or present
5	6 – 3	Absent or present

These scales may correlate with the physiological status e.g., patients who are Hunt and Hess grades 1 and 2 have near normal cerebral autoregulation and ICP.

These scales are also used to identify a baseline neurological status; therefore,

- Any acute change should be assessed.
- Failure of patients to return to the baseline after surgery needs more investigations to determine if the residual anesthetic effect or surgical intervention is the cause.

Management of Cerebral Aneurysm

1- Medical Treatment:

It is done before surgical clipping to avoid the increased transmural pressure of the aneurysm and thus, decreasing the incidence of aneurysmal rupture. Medical treatment includes:

- Strict blood pressure control to maintain systolic blood pressure < 160 mm Hg with esmolol or labetalol.
- Opioid for pain management.
- Lignocaine for tracheal suctioning if the patient is intubated.
- Stool softeners.

2- Surgical Clipping:

The ideal time for surgical clipping after subarachnoid hemorrhage is one of the following:

a- Early surgical clipping on the day "0" (ultra-early within 12 hours) or day "1". It is advocated in most centers.

Advantages:

1- Less risk of re-bleeding especially during HHH therapy (see later).

2- Less risk of vasospasm as it appears that vasospasm is related to the presence of blood near circle of Willis.

3- Less risk of prolonged bed rest complications such as deep venous thrombosis (DVT), atelectasis, and pneumonia as bed rest is indicated during medical treatment of vasospasm if late surgical intervention is indicated.

Disadvantages:

1- Surgical approach is more difficult because the brain is edematous, tight, and there is hydrocephalus.

2- Increased risk of intraoperative aneurysmal rupture due to the lesser period of time for clot to organize over the site of the initial bleeding.

b- Late surgical clipping on 11-14 days after subarachnoid hemorrhage.

It has a better outcome than early surgical clipping.

3- Endovascular Therapy: includes:

a- **Placement of** Guglielmi detachable thrombus-inducing **wire coils,** under general anesthesia in most cases, which causes thrombus formation. This obliterates the aneurysm. Now it is widely accepted especially in: poorly surgical candidates, and
surgically difficult aneurysms as basilar aneurysms.

b- **Balloon angioplasty** is tried for treatment of vasospasm.

c- **Aneurysmal trapping** where a clip is placed on the artery both proximal and distal to the aneurysm usually by means of the superficial temporal artery.

Complications:
- Hemorrhage.
- Thrombosis.
- Mal-positioning.

Anesthetic management of interventional neuro-radiology is discussed in the chapter of "Radiology".

Anesthetic Management of Subarachnoid Hemorrhage:

It is nearly the same as craniotomy aiming for brain protection in addition to avoiding aneurysmal rupture.

Preoperative Management:

Preoperative Evaluation:

1- Neurological Assessment: should be documented such as:
- Clinical picture of subarachnoid hemorrhage.
- The degree of severity of subarachnoid hemorrhage.

2- Presence of Coexisting Disease: such as hypertension, renal, cardiac or ischemic heart disease. They are **relative contraindications to elective hypotension.**

3- Drug Therapy: for precautions and side effects such as β-blockers and Ca^{++} channel blockers.

4- Preoperative Investigations:

Besides the standard investigations, CT scan, MRI, Lumbar puncture, 4-vessel angiography, and trans-cranial Doppler can be done.

Preoperative Patient Preparation:

The same preparations as that of **craniotomy** in addition to:
- Patient preparation is performed **in intensive care,** which includes:
  - Bed rest.
  - Mild analgesics (aspirin should be avoided due to its antiplatelet action).
  - Stool softeners to prevent straining.
  - Blood pressure control.
- Surgeries for subarachnoid hemorrhage are associated with **excessive blood loss**; therefore,
  - Multiple large bore venous **cannulas** should be inserted.
  - Intravenous **volume loading** should be done.
  - 3-4 units of whole **blood** should be available preoperatively.

Premedication:

It is the same principle of premedications as that of **craniotomy**.

Intraoperative Management:

Decision to **proceed or delay the surgery** depends on:

1) 50% of patients with subarachnoid hemorrhage have **increased CPK-MB fraction** and **troponin**. Also, they have **ECG changes** as non-specific T waves, canyon T waves, prolonged QT interval, ST segment depression, and appearance of U waves. These effects are usually due to extreme hypertension and

autonomic discharge which cause myocardial injury which is sub-endocardial. It is **not indicative of transmural myocardial infarction**. Therefore, the decision to proceed or postpone the surgery should be weighed against the risk of vasospasm and bleeding. In most cases, the risk of vasospasm and re-bleeding outweighs the risk of perioperative myocardial infarction. Furthermore, if coronary artery disease is present, these patients are not candidates for myocardial revascularization which requires heparinization.

2) Pulmonary edema or malignant arrhythmia postpones the surgery. It should be controlled before surgery.

Aim, monitoring, induction, position, and **maintenance** have the same principles as that of craniotomy (see before).

Hyperventilation is avoided in patients with vasospasm because:

- Hyperventilation decreases CBF which results in brain ischemia.
- Hyperventilation with nimodipine (used in treatment of vasospasm), produces additive effects with isoflurane resulting in severe hypotension.

Intraoperative Fluid Management:

- No need for fluid restriction (as other craniotomies), but the **calculated maintenance amounts** should be administered.
- Types and precautions of fluid management are discussed in craniotomy (see before).

Intraoperative Complications and Problems:

The same complications and problems **as those in craniotomy** such as brain protection, increased ICP, intraoperative hypertension, hypotension, bradycardia, hypothermia, and special problems of posterior fossa e.g., brainstem injury (**discussed above in details**).

In Addition to Measures of Brain Protection:

Deep hypothermic circulatory arrest may be required. It needs cardio-pulmonary bypass at body temperature (15-28 °C). It is indicated in:

- Giant aneurysms.
- Difficult basilar artery aneurysms.
- Anatomically complex aneurysms which are not clippable.

In Addition to Measures of Increased ICP:

A rapid decrease in ICP should be avoided before dural opening because it may promote **re-bleeding** by removing the tamponading effect of ICP on the aneurysm; therefore, mannitol should be given after dural opening.

Other Measures Specific for Craniotomy of Subarachnoid Hemorrhage include:

1) Controlled Hypotension (Induced or Elective):

Aim: to maintain MAP at a minimum of **60-70 mm Hg** in previously normotensive patients. It may be further decreased to 50 mm Hg only for a brief period if necessary.

Agents: (usually needed **after the dura is opened**) by:

- **Potent volatile** anesthetic agents.
- **Direct vasodilators** such as nitroglycerin or nitroprusside.
- **β-blockers** such as esmolol or labetalol.
- **Ganglion blockers** (trimethaphan).

Value:

- It provides a **slack aneurysm** to facilitate surgical clipping.
- It decreases the transmural pressure across the aneurysm **making rupture or re-bleeding less likely.**
- **It decreases blood loss** improving surgical visualization in the event of bleeding.

Disadvantages:

- **Cerebral perfusion** may be seriously **compromised** in the presence of vasospasm.
- **Rebound hypertension** due to prolonged hypotension where there are increased plasma levels of circulating vasoconstrictors.
- **No studies proved that hypotension decreased the incidence of intraoperative rupture** of aneurysms; therefore, its use should be reserved for:
  - brief periods around clip application.
  - treatment after intraoperative rupture.

Relative Contraindications:

- Hypertension.
- Ischemic heart disease.
- Cerebrovascular disease

• Renal disease.

Some centers **avoid controlled hypotension** in neurosurgery even in the face of intraoperative rupture, but other centers use it **only for short periods of time**.

2) Temporary Clip Occlusion (Aneurysmal Trapping):

Some authors call it **Regional Controlled Hypotension**

It is widely used now instead of generalized controlled hypotension.

Value: to produce a slack aneurysm to: ▫ facilitate placement of a permanent clip.
▫ decrease the incidence of intraoperative rupture of the aneurysm.
▫ decrease the requirement for generalized controlled hypotension.

Methods:

• Placement of a temporary clip on one or more parent vessel e.g., to place a permanent clip on an anterior communicating artery aneurysm, a temporary clip is placed on the right or left anterior cerebral artery, or both.

• The maximal duration of temporary clip occlusion before occurrence of neurological deficit is unknown, but some authors recommend to be left **for 10 minutes** with barbiturate infusion. It is related to:

▫ The location of the aneurysm.
▫ The distribution of perforating vessels distal to the temporary clip (the white matter and major deep nuclei are more susceptible to temporary ischemia than the grey matter).

Disadvantages:

The main complication after temporary clip occlusion is **neurological deficits**. Risk factors increasing neurological deficits include:

• Poor preoperative neurological status.
• Age > 61 years old.
• Distribution of the perforating vessels in the horizontal and distal segments of middle cerebral artery.

3) Intraoperative Rupture of Cerebral Aneurysm:

Incidence: 2-20%.

Prevention: Precise control of transmural pressure is important in preventing aneurysm rupture.

Transmural pressure = CPP = MAP – ICP or CVP (whichever is greater).

Outcome: The stage of the operation at which rupture occurs affects the outcome as:

• **Rupture** of cerebral aneurysm at the **induction** of anesthesia has the **worst outcome** with a high mortality rate **75%.**

• **Rupture** during **surgical dissection** has **a better outcome** with low mortality rates.

Clinical Suspicion:

A sudden increase in ICP causes sudden sustained hypertension with/without bradycardia (**Cushing reflex**) which is suggestive of rupture.

Management:

a- If rupture occurs during induction

1- **Controlling ICP** and maintaining CPP are done first.
2- The surgery is usually **postponed** to allow reassessment of neurological status and prognosis.

b- If rupture occurs during surgical dissection:

Control of bleeding while maintaining systemic perfusion is done by:

• **Temporary clip placement**.
• **Controlled hypotension** to mean blood pressure of 40-50 mm Hg (if the temporary clip is not effective to stop bleeding). Some centers avoid this technique at all.
• **Ipsilateral carotid compression** for brief periods may be necessary.

If bleeding cannot be controlled in a timely fashion and significant amounts of blood accumulate in the subarachnoid space, severe brain swelling that is refractory to all treatments may ensue.

4) Vertebro-Basilar Aneurysms:

There are special problems as: • Risk of venous air embolism.
• Brainstem injury.

So, auditory evoked potentials, cardiovascular system monitors, and spontaneous ventilation (for detection of apnea and gasping) are essential and needed.

Emergence:

The patients are either:

a) **Left intubated** with a muscle relaxant, controlled ventilation, and sedation. It is indicated in:

• Patients who are grade IV or V (± III) in Hunt and Hess scale.

• Patients with vertebral or basilar aneurysms secondary to cranial nerve damage because there is loss of protective airway reflexes.

b) **Extubated** at the end of surgery in operating room. It is indicated in:

• Patients in grade I or II (± III) in Hunt and Hess scale.

Smooth extubation is performed (see before).

Postoperative Management and Intensive Care Considerations:

The patient is usually transferred to an **intensive care unit** for close monitoring, postoperative care, and postoperative complications which are the same as these of craniotomy (see above).

Additional **postoperative complications include:**

1- Delayed Recovery:

Causes:

a- Anesthetic causes: • Residual effects of: ▫ inhaled or i.v anesthetics,
▫ nondepolarizing muscle relaxants, or
▫ opioids or benzodiazepines.
• Hypothermia: It may prolong the effects of i.v anesthetics.
• Hypoxia, hypercarbia, hyponatremia, or hypoglycemia; so, arterial blood gases are needed.

b- Surgical: • Subdural hematoma.
• Intra-cerebral hemorrhage.
• Hydrocephalus.
• Pneumocephalus.
• Cerebro-vascular occlusion.

Therefore, CT scan or angiography is needed.

Treatment: of cause.

2- Cerebral Vasospasm (Delayed Ischemic Neurological Deficit "DIND")

Definition:

It is **segmental or diffuse narrowing** of the lumen of one or more intracranial arteries. Its severity is related to the amount and location of subarachnoid blood. Diffuse cerebral vasospasm carries **the worst prognosis.**

Incidence:

• Clinically: 30% of patients with subarachnoid hemorrhage.

• Angiographically: 60% of patients with subarachnoid hemorrhage even without clinical picture.

Pathogenesis:

The exact mechanism is unknown, but development of vasospasm is mainly related to the contact of free hemoglobin with the luminal surface of cerebral arteries.

Pathophysiological Changes:

1- There are several mediators involved such as:

• O_2 radicals theory; where oxy-hemoglobin leads to production of superoxide radicals which decrease the production of nitric oxide in endothelial cells. This increases protein kinase C activity and intracellular Ca^{++} which in turn cause myofilament activation and vasospasm.

• Other inflammatory mediators such as eicosanoids (prostaglandins), endothelin (cause vasoconstriction), interleukin I, and immune complexes are increased.

2- Structural changes:

• Leukocytes, red blood cells, and macrophages are seen in the vessel walls.

• Degenerative changes in the intima and media of blood vessels with smooth muscle proliferation, collagen deposition, and eventually thickening of the vessel wall occur.

3- Functional changes:

• Cerebral autoregulation is impaired and CBF in some areas appears to be pressure dependent.

Clinical Picture:

It occurs within **4-12 days** after subarachnoid hemorrhage. Then it resolves **11-14 days** after sub-arachnoid hemorrhage. There are:

• Altered level of consciousness (disorientation and drowsiness).

• New onset of focal neurological deficit.

• Increased headache, meningism, and fever.

• Cardiovascular and respiratory changes if vessels in posterior fossa are involved.

Investigations:

1- Trans-Cranial Doppler:

It should be performed daily at bedside to detect the onset of cerebral vasospasm to start the triple-H therapy (see later). It detects CBF velocity as follows:

- If CBF velocity is **< 100 mL/sec**, cerebral vasospasm is **unlikely.**
- If CBF velocity is **> 120 mL/sec** with **new focal neurological deficit, diagnosis** of cerebral vasospasm can be made. However, the trend of values over time is more important than the absolute value.
- If CBF velocity is **> 200 mL/sec, severe** cerebral vasospasm occurs which is associated with high risk of cerebral infarction.

2- Cerebral Angiography:

It is the **gold standard** for diagnosis of cerebral vasospasm. It should be done to confirm diagnosis, number and location of vessels involved.

It is **positive in 60%** of patients after subarachnoid hemorrhage. Only 50% of them show a clinical picture. (i.e., 30% of all subarachnoid hemorrhagic patients).

Differential Diagnosis:

• Re-bleeding • Hydrocephalus • Seizures • Hyponatremia • Drug effect.

Management:

A) Prophylaxis:

1- Ca^{++} Channel Blockers:

It is the standard prophylactic therapy to prevent cerebral vasospasm.

The mechanism is unknown, but may aid in **maintaining cellular integrity by preventing Ca^{++} influx into the cells.**

Agents:

- **Nimodipine (oral):** It should be initiated on the first day and continued **for 21 days** after subarachnoid hemorrhage. It does not improve the overall incidence of vasospasm, but it improves the incidence of severe vasospasm. It does not improve the mortality, but improves the outcome for survivors.
- **Nicardipine (i.v.):** It improves the incidence of symptomatic vasospasm, but it does not improve the outcome.

Complications: The main complication is **hypotension**; therefore, it is difficult to achieve hypertensive, hypervolemic, hemodilution (HHH) therapy.

2- Other Measures:

- **Removal of subarachnoid blood** as **quickly** as possible.
- Instillation of **thrombolytic agents** (e.g., urokinase), but this may increase the likelihood of re-bleeding.
- Decrease the inflammatory response by inhibiting iron dependent lipid peroxidation such as:
  - Glucocorticoid: It does not prevent cerebral edema after rupture.
  - 21-aminosteroids (Tirilizad).
  - Ibuprofen.
  - TAK-044: It is endothelin antagonist (under research).

B) Treatment:

1- Continuation of prophylactic therapy.

2- Hypertension, Hypervolemia, Hemodilution Therapy (HHH Therapy):

Aim: To improve CBF to pass the stenotic areas.

Technique: Aggressive hypervolemia and hypertension by:

a- **Intravascular volume expansion** with crystalloids or colloids to increase cardiac output.

These fluids should be **isotonic** and should contain enough Na^+ to avoid hyponatremia.

Vasopressin or fludrocortisone may be added to avoid excess fluid and Na^+ loss.

b- **Vasoactive infusions e.g., dopamine and dobutamine** are used if hypervolemia alone is inadequate.

Recommended Target Values:

The triple-H therapy is continued until the following parameters are reached:

- Central venous pressure (CVP) = 10-12 mm Hg.
- Pulmonary capillary wedge pressure (PCWP) = 15-18 mm Hg.
- Cardiac index = 3-3.5 L/min/m^2.
- Hematocrit = 30% - 35%.

- Arterial blood pressure = various target values that have been reported, but a reasonable plan is suggested as follows:
  - If the aneurysm is **clipped,** increase systolic blood pressure up to 160-200 mm Hg.
  - If the aneurysm is **unclipped**, increase systolic blood pressure up to 120-150 mm Hg.

End Point of Therapy: Triple-H therapy should be stopped if one of the following occurs:

- Resolution of the neurological deficit, or
- Occurrence of complications of therapy such as:
  - Myocardial ischemia.
  - Pulmonary edema (especially with nimodipine as it causes myocardial depression).
  - Re-bleeding or rupture of a secondary aneurysm.

3- Other Measures:

- **Intra-arterial infusion of verapamil or other vasodilators**.
- **Angioplasty** via balloons.

Both are usually reserved for cases that fail to respond to HHH therapy.

3- Hydrocephalus:

Treatment: If it is acute, emergency ventricular draining is needed.
If it is chronic, delayed ventricular shunting is needed.

4- Cerebral Salt Wasting Syndrome (and Hyponatremia):

Causes: **1- A syndrome-like the syndrome of inappropriate ADH secretion:** due to release of **cerebral natriuretic factor** from the hypothalamus secondary to distension of cerebral ventricle due to hydrocephalus. This factor is similar to but may not be the same as that released from the heart. This syndrome causes extracellular volume contraction and renal loss of Na^+ resulting in hyponatremia which may cause brain swelling.

N.B.: **Syndrome of Inappropriate ADH Secretion:** There is excessive release of ADH resulting in volume expansion. It is treated by fluid restriction.

2- Prolonged or excessive mannitol use:

Treatment: It is treated by isotonic or hypertonic saline solution. Do not perform fluid restriction as it may precipitate vasospasm.

5- Neurogenic Pulmonary Edema:

Due to postoperative increase in sympathetic activity.

6- Increased ICP:

It is managed as before.

7- DVT and Pulmonary Embolism:

It is managed as before.

Anesthetic Management of Coil Placement and Interventional Neuro-radiology

It is nearly the same as that of craniotomy for aneurysm resection. It can be performed under sedation or general anesthesia. Mild sedation has the advantages of the ability to perform intra-procedural neurologic examination, but general anesthesia is more preferred because patient movement during sedation may produce the risk of aneurysm rupture or inappropriate coil dislodgement resulting in coil embolization. Details of anesthetic management are discussed in the chapter of "Radiology".

Anesthetic Management of Arterio-Venous Malformation (AVM)

AVM is dilated arteries and veins with no intervening capillaries. Craniotomies are not urgent unless the AVM or a resulting hematoma is causing pressure effects (figure 15-22).

Anesthetic Problems:

- If it ruptures, it causes **intracerebral subarachnoid hemorrhage** usually at the age of 10-30 years.
- If it grows, it increases **ICP** and may be associated with **seizures**.
- If it is large, it causes **high cardiac output failure**.
- If there is high blood flow through such lesions, it may **"steal" blood from surrounding tissues** leading to relative ischemia. **When the lesion is excised, a relative hyper-perfusion** of surrounding tissues may occur resulting in cerebral edema and increased ICP.

• **Hypotensive anesthesia** may be indicated.
• Extracorporeal membrane oxygenation (ECMO) may be needed in large AVM with deep hypothermic circulatory arrest.

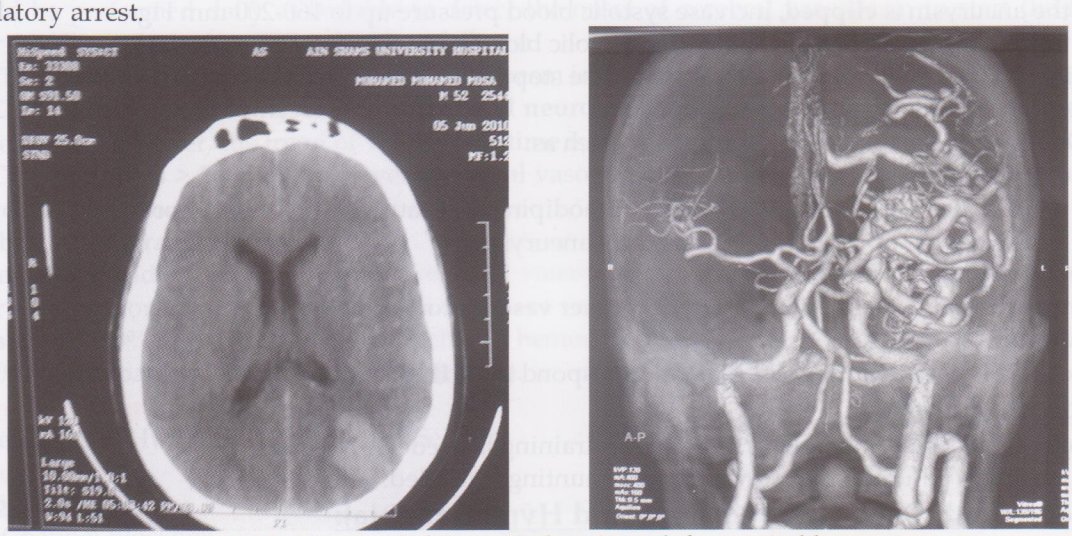


Figure 15-22: CT scan (left image) showing a left occipital hematoma.
CT angiography (right image) showing an underlying AVM

Moyamoya Disease

It is a progressive stenosis of intracranial vessels with the secondary development of an anastomotic capillary network. The affected vessels have a thickened intima and a thin media with associated intracerebral aneurysm.
Moyamoya is the Japanese term for "puff of smoke" and refers to the angiographic finding of a cluster of small abnormal blood vessels.

Causes:

1- Familial.
2- After head trauma.
3- In association with other disorders such as neurofibromatosis, tuberous sclerosis, and fibro-muscular dysplasia.

Clinical Pictures:

• In children; there are usually symptoms of cerebral ischemia, such as transient ischemic attacks and infarcts.
• In adults; there are usually symptoms of hemorrhagic complications such as strokes.

Investigations:

1- Conventional angiography (figure 15-23).
2- Magnetic resonant angiography demonstrating a cluster of small abnormal blood vessels.
3- CT scan.

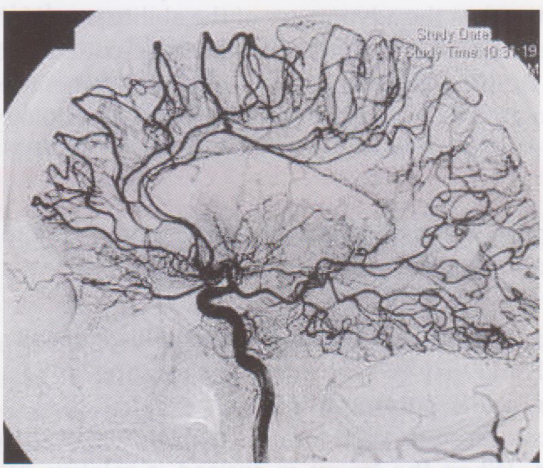


Figure 15-23: Cerebral angiography, lateral view showing prominent cortical collaterals of Moyamoya disease.

Treatment:

1- Medical treatment: vasodilators and anticoagulants.

2- Surgical treatment: includes direct anastomosis of the superficial temporal artery to the middle cerebral artery (also known as extracranial-intracranial bypass).

Anesthetic Management:

It is similar to **craniotomy with brain protection** with maintaining hemodynamic stability.

Anesthesia for Head Injury (Head Trauma)

Head injury contributes to 50% of deaths due to trauma.

Types:

In head injury, many structures can be injured. These injuries are considered **primary head injury** (i.e., they occur at the time of impact). These injuries include:

1- Scalp Lacerations: It causes significant blood loss up to hypovolemic hemorrhagic shock.

2- Skull Fractures: Presence of skull fractures increases the likelihood of a significant intracranial lesion. Skull fractures include:

a- Linear Skull Fractures: They are commonly associated with epidural or subdural hematoma. Basilar skull fracture may be associated with CSF rhinorrhea, otorrhea, pneumocephalus, cranial nerve palsies, or even a cavernous sinus rupture. Carotid artery fistula, hemotympanum, or ecchymosis into peri-orbital tissues (**raccoon's sign**) or behind the ear (**battle's sign**) may occur.

b- Depressed Skull Fractures: They are often present with an underlying brain contusion which may be limited to the brain surface or may involve hemorrhage into the deeper hemispheric structures or the brainstem. It is called **compound fracture** if it is associated with laceration of the overlying scalp.

c- Maxillo-Facial Injury.

d- Mandibular Fracture: It is discussed in details in the chapter of "Trauma".

3- Intracranial Injury (Brain Injury):

Brain injuries are either:

a- Coup injury: that occurs directly under the injury site.

b- Contrecoup injury: that occurs in intracranial regions opposite the point of impact. Contrecoup injury occurs because the brain may move relative to the skull and dura causing compression of the brain remote from the site of impact.

Brain injuries include:

1- Brain Concussion: It is an episode of transient loss of consciousness following cranio-cerebral trauma. There is no evidence of pathological brain damage. Patients may suffer from variable degrees of memory loss, autonomic dysfunction, headache, tinnitus, and irritability.

2- Brain Contusions: They are heterogeneous areas of hemorrhage into the brain parenchyma and may produce neurological deficits depending on their anatomical location. Contusions are often associated with disruption of the blood brain barrier and may be complicated by extension of the hemorrhage, edema formation, seizures, increased ICP or brain herniation especially with large contusions.

3- Intracranial Hematomas: Large hematomas may cause increased ICP and brain herniation which requires surgical evacuation. Hematomas may also develop postoperatively. Intracranial hematomas are: **a- Epidural Hematoma:** commonly develops due to injury of the middle meningeal artery and usually results in rapid profound neurological deficits. Hematoma usually takes a homogenous lentiform configuration.

b- Subdural Hematoma: It occurs due to tearing of bridging veins that drain from the cortex to the dura and superior sagittal sinus. It has a worse prognosis than epidural hematoma. Because it is not surrounded by dural attachments, the hemorrhage often spreads diffusely across the cortical surface resulting in a crescent-shaped image on CT scan. It has more slow and insidious onset.

c- Subarachnoid Hemorrhage: The subarachnoid bleeding itself does not usually cause neurological damage, but hydrocephalus and cerebral vasospasm which are delayed complications, can lead to neurological impairment.

d- Diffuse Axonal Injury: It is shearing of brain tissue with disruption of neuronal axon projections in the cerebral white mater resulting from rotational deceleration of the brain. This diffuse injury to axons occurs microscopically and can result in severe neurological impairment. Evidence of diffuse axonal injury is often not demonstrable on CT scan. However, macroscopic hemorrhagic lesions can

be seen in deep brain structures such as the corpus callosum or brainstem in association with diffuse axonal injury.

N.B.: **Non-Accidental Brain Trauma (Shaken Baby Syndrome)** occurs due to excessive shaking of a baby.

Management:

The choice between medical and surgical management of head trauma depends on radiographic and clinical findings. Operative treatment is usually elected for:

- Depressed skull fractures.
- Evacuation of epidural, subdural and some intracranial hematomas.
- Debridement of penetrating injuries.

Pathophysiology of Brain Injury

A) Primary Brain Injury:

It is the **direct result of the disruptive forces** occurring **at the time of impact**.

B) Secondary Brain Injury:

It is the **ischemic brain injury** which occurs **after the initial (primary) trauma** to the brain.

Mechanism:

It is assumed to be **ischemic in origin** due to either secondary intracranial insult or secondary systemic insult.

a- Secondary Intracranial Insult:

Intracranial hypertension occurs due to:

- Delayed intracerebral hematoma as subdural or epidural.
- Vasogenic cerebral edema.
- Cerebral hyperemia.
- Carotid artery dissection.
- Seizures.
- Vasospasm.

Intracranial hypertension results in decreased CBF to the threshold of cerebral ischemia i.e., < 18 mL /100 g brain tissues/min.

b- Secondary Systemic Insult:

These are systemic extracranial factors that occur after brain injury which cause more brain insult. They include:

1- Hypotension: It is the most important factor. It may occur due to:

- Excessive bleeding and shock.
- Myocardial infarction or contusion.
- Pericardial tamponade.
- Spinal cord injury.
- Tension pneumothorax.

Hypotension alone is associated with a 150% increase in mortality rate in patients with significant head injuries. The associated cerebral autoregulation (as discussed above) makes cerebral blood flow directly related to systemic arterial pressure. Thus, if hypotension occurs, reduced tissue perfusion and ischemia may result.

2- Hypoxia: It is another very important factor. It may occur due to:

- Respiratory arrest.
- Airway obstruction.
- Acute respiratory distress syndrome (pulmonary edema).
- Aspiration pneumonia.
- Pneumonia and hemothorax.
- Pulmonary contusion.

3- Other associated factors that can increase brain insult:

- Electrolyte imbalance (diabetes insipidus or syndrome of inappropriate anti-diuretic hormone).
- Anemia.
- Hyperthermia.
- Hypercapnia.
- Hypoglycemia.
- Coagulopathies.

Elective surgery for extracranial injuries should be delayed as long as possible due to these extracranial systemic factors which should be corrected before any elective surgery.
Monitoring and managing of **cerebral oxygenation** (brain tissue PO_2) and **cerebral perfusion pressure** are essential in preventing secondary brain injury.

Anesthetic Management:

Preoperative Management:

Preoperative Evaluation and Preparations:

1- Initial Resuscitation:

For patients with severe head injury, ideally initial resuscitation should begin in the emergency department by "**ABCDE" protocol.**

"**A** and **B**" **A**irway and **B**reathing resuscitation:

In severe head injury, there is commonly airway obstruction and hypoventilation resulting in hypoxemia in 70% of patients with/without hypercarbia. This further increases ICP. It is managed by **tracheal intubation** which is usually needed in severe head injury.

Special precautions:

- All patients with head injury or major trauma should be regarded as having **cervical spine injury** (the incidence is 10%) until proved otherwise radiologically; therefore, **in-line stabilization** should be used during airway manipulation to maintain the head in the neutral position.
- All patients should be regarded as having **full stomach** with a risk of pulmonary aspiration; therefore, **cricoid pressure** should be maintained during mask ventilation.

Methods of intubation:

- Adequate preoxygenation with 100% O_2 should be performed.
- The pressor response of intubation should be avoided. It is discussed in full details in the chapter of "Airway Management".
- **Rapid sequence crush induction** is done. Some anesthesiologists consider patients with **increased ICP** to have an increased risk of aspiration due to the presence of vomiting; therefore, crush induction is commonly indicated in these patients.
- **Induction agents and muscle relaxants such as suxamethonium** are used with certain precautions (discussed before with craniotomy). **Rocuronium** is a suitable alternative.
- **The endotracheal tube** should be **armored** latex (non-kinkable) tube, and should be **well secured**, and **re-checked after positioning**.
- **In difficult intubation** cases, one of the following can be used; awake intubation, blind nasal intubation, fiberoptic intubation, and tracheostomy.

Blind nasal intubation is contraindicated in patients with: basilar skull fractures.
maxillofacial injuries.

"C" Circulation resuscitation:

Patients with head injuries may present with **hypotension (and hypovolemic shock)** which is more common due to: • other associated injuries as thoraco-abdominal injuries.
and • scalp lacerations especially in children.

Hypotension causes a **marked decrease in CPP** especially if associated with increased ICP resulting in neuronal damage.

Management:

Hypovolemic shock should be **managed first** even before neurological assessment. **Maintaining CPP** by normalization of the mean arterial blood pressure and correction of hypoxia is the main factor in decreasing morbidity and mortality.

a- Intravenous Fluids:

- Colloids and blood transfusion, to maintain Hct >30%, are preferred to crystalloid solutions in preventing cerebral edema.
- Hypertonic saline (3 or 7.5%) draws water from the intracellular space allowing:
  - restoring blood volume in a traumatized patient

and - decreasing brain edema which in turn decreases ICP (effective as mannitol 20%).

Hypertonic saline cannot be used for long periods due to its side effects.

Hypovolemic shock and hypertonic saline are discussed in more details in the chapter of "Cardiovascular Disease".

• Avoid hypotonic solutions e.g., lactated ringer solution and glucose-containing solutions.

b- Vasopressors e.g., dopamine.

Hypertension may occur in **patients** with head injuries without **massive blood loss**. It is primarily due to:

• intense sympathetic nervous system activity

and • marked circulatory catecholamines.

Considerable debate is found regarding significance of hypertension:

• Some authors believe that cerebral perfusion is optimized because high arterial pressure opposes the effects of increased ICP.

• Some other authors believe that in the presence of disrupted blood brain barrier, hypertension will cause marked extravasation of edema fluid aggravating cerebral edema and result in a further increase in ICP.

"D" Defibrillator or Disability:

• **Defibrillator:** should be available.

• **Assessment of neurological disability** should be done rapidly and documented.

"E" Exposure:

• Exposure for a complete secondary survey and to treat associated injuries as required.

2- Neurological Assessment:

1) Presence of increased ICP and its management as before.

Increased ICP < 20 mm Hg is associated with mortality 20%.
Increased ICP > 20 mm Hg is associated with mortality 50%.
Increased ICP > 40 mm Hg is associated with mortality 75%.
Increased ICP > 60 mm Hg is associated with mortality 100%.

The management of increased ICP should be started preoperatively or in intensive care (as before).

N.B.: Most head injury protocols call for empiric administration of i.v. mannitol as soon as the patient arrives to the emergency room. It was thought before that mannitol could aggravate the increase in ICP by diffusing through the disrupted blood brain barrier and inducing additional cerebral edema which proved later to be wrong.

2) Assessing the level of consciousness by Glasgow Coma Scale (GCS)

Category	Score
1- Eye opening:	
• Spontaneous	4
• To verbal command	3
• To pain	2
• No response	1
2- Best motor response:	
• To verbal command: Obeys	6
• To pain - Localization of pain	5
- Normal flexion withdrawal	4
- Abnormal spastic flexion (Decorticate rigidity)	3
- Extensor response (Decerebrate rigidity)	2
- No response	1
3- Best verbal response:	
• Oriented & converse	5
• Disoriented & converse (confused)	4
• Inappropriate words	3
• Incomprehensive sounds	2
• No response	1

The highest score is 15 and the lowest score is 3

Mild head injury is GCS 13-15 (80% of cases).
Moderate head injury is GCS 9-12 (10% of cases).
Severe head injury is GCS 3-8 (10% of cases): These patients are in deep coma and show 35-50% mortality or remain in vegetative states.

GCS is suitable for age > 5 years old.

Pediatric Coma Scale (for ages < 5 years old)

The eye opening response is the same as for adults, the motor and verbal responses are modified for age as shown in the following table.

Category	Score
1- Eye opening: The same as GCS.	1-4
2- Best motor response (upper limb): The same as GCS.	
• To verbal command: Obeys (for > 2 years age)	6
• To pain - Localization of pain (for < 2 years age)	5
- Normal flexion withdrawal (for > 6 months)	4
- Abnormal spastic flexion (Decorticate rigidity) (for < 6 months)	3
- Extensor response (Decerebrate rigidity)	2
- No response	1
3- Best verbal response:	
• Smiles, oriented to sounds (for > 5 years age)	6
• Follows objects, interacts (for > 5 years age)	5
• Consolable, inappropriate words (for > 1 year age)	4
• Inconsistently consolable, moaning sounds (for > 6 months)	3
• Inconsolable, irritable, and cries (for < 6 months)	2
• No response	1

The highest score of the pediatric coma scale is 9 at 0-6 months age.
11 at 6-12 months age.
13 at 1-2 years age.
14 at 2-5 years age.

Signs of increased mortality:
- GCS ≤ 8 (in adults).
- Midline shift > 5 mm.
- Large lesions > 25 mL.
- Ventricular compression on CT scan.

Generally mortality in children with severe head injury is less than in adults.

3) Sensory or motor deficits e.g., unilateral non-reactive dilated pupil indicates an expanding hematoma.

4) Presence of muscle wasting (for hyperkalemia).

5) The Classic Cushing Triad: Hypertension, bradycardia, and respiratory disturbances are unreliable because they occur **late** after brain herniation.

6) Signs of tonsillar herniation:
- Early the level of consciousness may be normal because the upper brainstem and reticular activating system remain intact.
- Nuchal rigidity.
- Abnormal gag and cough reflexes indicating medullary compression.

7) Assessment of brainstem function as respiratory pattern, pupil size and reactivity, and brainstem reflexes such as gag reflex, cough reflex, oculo-cephalic reflex (doll's eye maneuver), or oculo-vestibular reflex (cold caloric test).

8) Lateralizing signs present in presence of an expanding hematoma include:
- Unilateral papillary dilatation.
- Asymmetric posture.
- Hemiparesis.
- Facial weakness.

3- Presence of Associated Injuries (in 10-40%) such as intra-abdominal injuries, spine fractures, maxillo-facial and mandibular trauma, long bone fractures, and thoracic injury.....etc.

4- Presence of Associated Complications such as:
- Disseminated intravascular coagulopathy **(DIC)** in severe head injury due to release of large amounts of brain thromboplastin into the systemic circulation which activate the coagulation cascade.
- Adult respiratory distress syndrome **(ARDS).**
- Neurogenic pulmonary edema that may also contribute to acute pulmonary dysfunction due to overactivity of sympathetic nervous system resulting in pulmonary vasoconstriction.
- **Diabetes insipidus**: due to injury of the pituitary stalk.

- **Post-traumatic seizures (PTS):** They are either:

  Early: within 7 days of injury, mostly within the first 24 hours.

  Late: after 7 days of injury.

  Risk Factors: ▫ GCS < 10. ▫ Cortical contusion.
  ▫ Depressed skull fracture. ▫ Intracerebral hematoma.
  ▫ Penetrating head wound. ▫ Seizures within 24 hours of injury.

  Prophylaxis: Phenytoin and carbamazepine are used as a prophylaxis for one week. They protect against the early, but not the late seizures.

- **Electrolyte disturbances** such as:

1- Hyponatremia due to - mannitol administration or
- syndrome-like syndrome of inappropriate anti-diuretic hormone secretion (SIADH) (cerebral salt wasting syndrome) (see later).

2- Hypernatremia due to - enteral tube feeding,
- diuresis with mannitol, or
- diabetes insipidus.

3- Hypokalemia due to - diuretics.
- syndrome-like syndrome of inappropriate anti-diuretic hormone secretion (SIADH) (cerebral salt wasting syndrome).

4- Hypomagnesemia: that can aggravate hypokalemia and neurological insult because Mg^{++} reduces the neurotoxic effect of glutamate. The glutamate causes Ca^{++} influx which results in secondary brain injury and cell death.

5- Presence of Coexisting Diseases e.g., hypertension, diabetes mellitus, or ischemic heart disease.

6- Drug Therapy.

7- Preoperative Investigations:

The choice between surgical and medical treatment of head injury is based on radiological as well as clinical findings.

Critically ill patients should be monitored during investigations and uncooperative patients may need general anesthesia.

a- Investigations for Brain Injury:

1- Plain X-ray:

Figure 15-24.

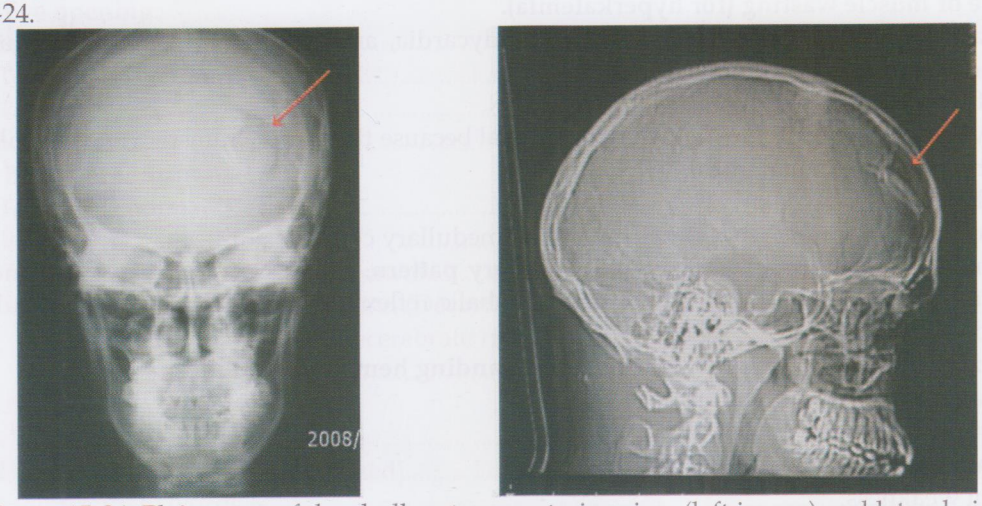


Figure 15-24: Plain x-ray of the skull, antero-posterior view (left image) and lateral view (right image), of the same patient, showing a left frontal depressed skull fracture

2- CT Scan: of the head, neck, and thorax.

- CT scanning is the **most important** investigation in head injury because it is **more accurate** than conventional radiographs (figure 15-25, 15-26, 15-27, 15-28, 15-29, 15-30, and 15-31).
- It should be done **as soon as possible.** It is indicated in any patient with head trauma with:
  - **GCS < 15.**
  - Nausea or vomiting.
  - Deficits in short-term memory.
  - Seizures.

• CT scan can delineate parenchymal hemorrhage and contusions, epidural and subdural hematomas, cerebral edema, hydrocephalus, and cerebral infarction.
• Surgical indications according to CT scan is indicated by evidence of an intracranial hematoma that causes compression of the ventricle or a midline shift of greater than 5 mm.
• Portable CT scanners are now available in some hospitals that enable the diagnostic study to be performed without transporting an unstable patient and risking harmful respiratory and cardiovascular effects.

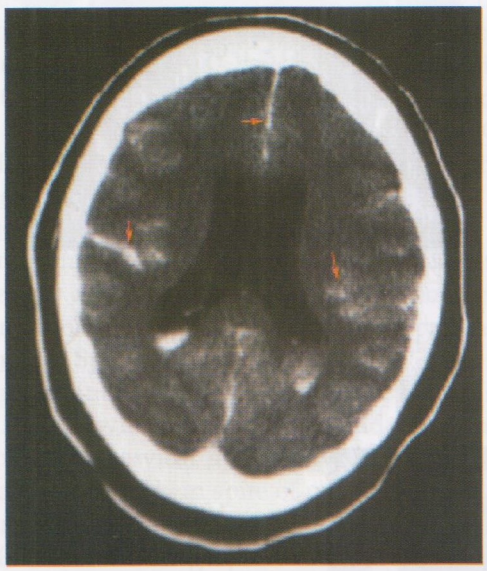


Figure 15-25: CT brain showing increased density in brain sulci denoting subarachnoid hemorrhage.



Figure 15-26: CT brain showing a peripheral high-density biconvex blood collection bounded by sutures, denoting epidural hematoma. Scalp hematoma is also present.

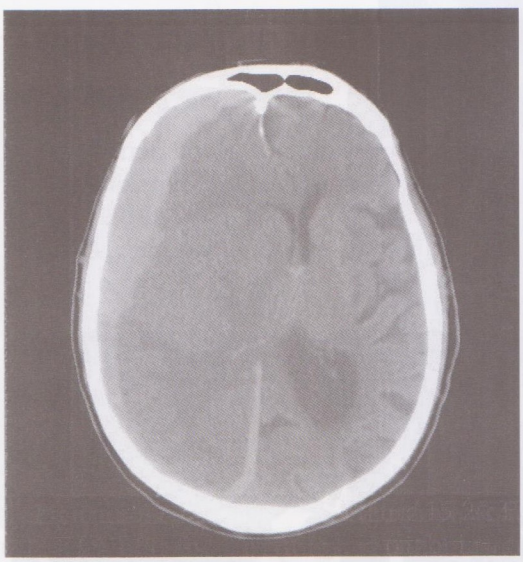


Figure 15-27: CT brain showing a peripheral high-density extra-cerebral collection within the subdural space compressing and displacing the right cerebral hemisphere denoting an acute subdural hematoma

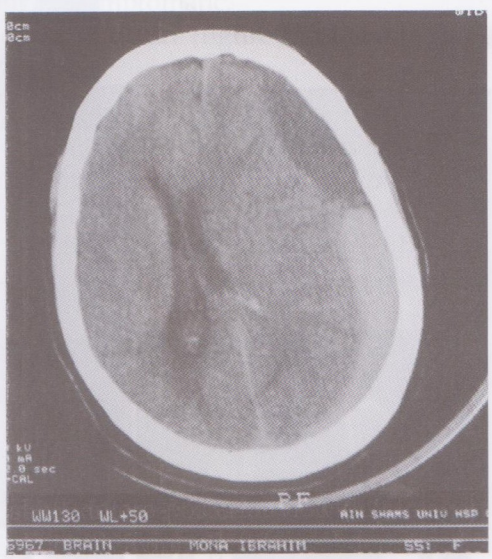


Figure 15-28: CT brain showing a left sided subdural hematoma. The upper part appears hypodense (blacker in color in comparison to normal brain); a chronic subdural hematoma. The lower part appears hyperdense (more white in color); acute subdural hematoma

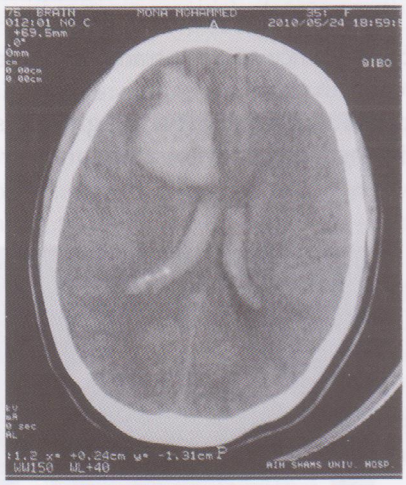


Figure 15-29: CT brain showing increased density within the right frontal brain parenchyma and both lateral ventricles denoting an intracerebral parenchymal hematoma and intra-ventricular hemorrhage

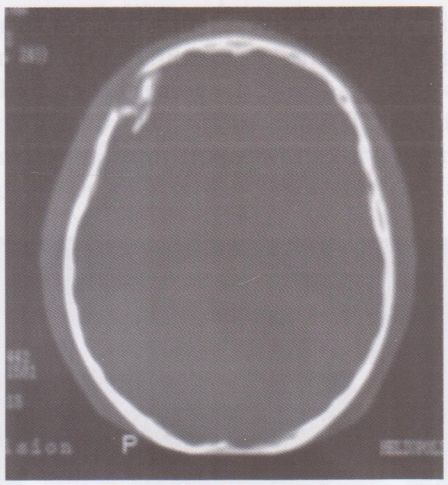


Figure 15-30: Axial CT brain (bone window) showing a depressed fracture of the skull

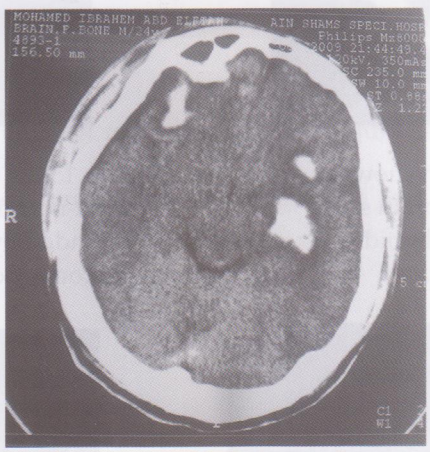


Figure 15-31: Axial CT brain showing multiple hyperdense areas of fresh blood density in the right frontal and left temporal lobes denoting bilateral hemorrhagic contusions

3- MRI: Generally, it is not available during emergency situations of head trauma especially in intubated patients (figure 15-32).

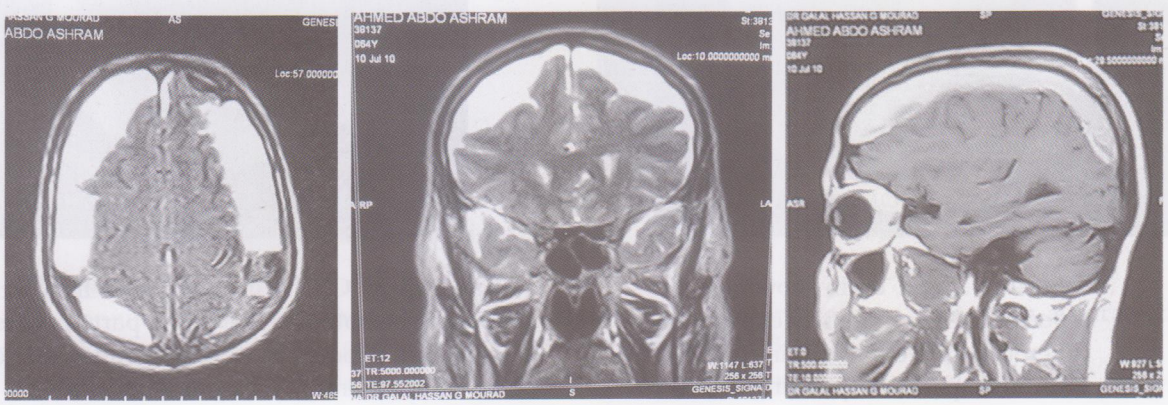


Figure 15-32: Axial, coronal, and sagittal MRI views (from left to right respectively) showing bilateral subdural hematoma

4- Cerebral Angiography: is mainly used to assess vascular disorders such as dissection or traumatic pseudo-aneurysm of the internal carotid or vertebral arteries and cerebral vasospasm.

5- Transcranial Doppler Ultrasonography:

It is a noninvasive technique that measures blood flow velocity in cerebral arteries and can diagnose cerebral vasospasm (see above). It can help in diagnosis of brainstem death by indicating absence of blood flow.

6- Monitoring of Intracranial Pressure: Although it is **not routinely** done, it is performed in cases with increased ICP by a small catheter inserted by the neurosurgeon under local anesthesia either into lateral ventricle (ventriculostomy), over the cerebral cortex, in the subdural space, or the epidural lumbar space (the most common). Ventriculostomy also is used to withdraw some CSF to decrease ICP. ICP monitoring is discussed in more details in chapter "Monitoring during Anesthesia & Intensive Care".

N.B.: Lumbar puncture (may be needed for CSF examination in patients with meningitis) should be avoided in patients with head trauma due to the risk of tonsillar herniation.

b- Investigations for the Associated Injuries:

1- Chest X-ray:

It is important to detect pulmonary, cardiac, airway, and vascular injuries.

If there is any doubt regarding pulmonary contusions, **a chest tube** should be placed before tension pneumothorax occurs particularly if the patient is going to receive positive pressure ventilation.

2- Cervical Spine X-ray:

It is important to detect cervical spine injury (sub-laxation, fracture) (figure 15-33) which requires head stabilization with skull fixation and traction. It should be initiated prior to airway manipulation. Radiology of cervical spine may not show fracture and patients may still have dangerous unstable cervical spine injury in spite of normal radiological images because:

- Injuries in atlanto-occipital region are especially difficult to identify radiologically.
- 26% of lateral radiographs have failed to show fracture.
- Even in the face of normal radiographic study, patients may still have significant ligamentous injuries.

Therefore, cervical spine palpation for tenderness is important in cooperative patients. In uncooperative or unconscious patients, the cervical spine should be considered not cleared even in light of normal x-rays. The cervical spine is considered clear only if:

- there is no radiological evidence.
- the mental status is normal.
- the patient is asymptomatic.

3- Cervical Spine CT scan and MRI: can be used to diagnose spine fracture (figure 15-34 and figure 15-35).



Figure 15-33: Plain x-ray lateral view cervical spine showing fracture dislocation of the second cervical vertebra

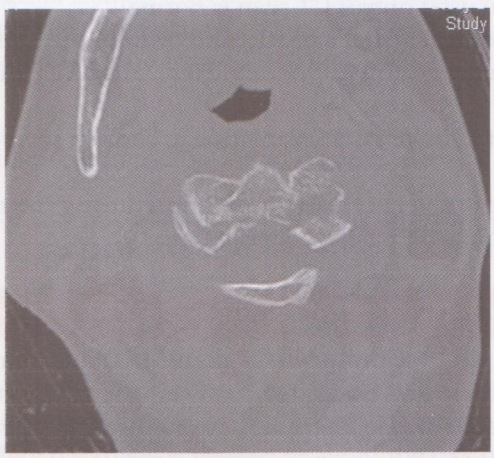


Figure 15-34: Axial CT of cervical vertebra showing fracture of the vertebral body

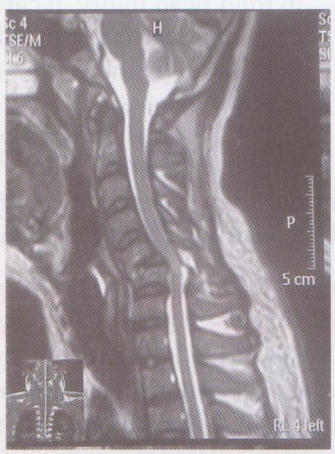


Figure 15-35: MRI cervical spine showing sublaxation

4- Diagnostic Peritoneal Lavage.

5- Abdominal Ultrasonography:

6- ECG: shows T wave, ST segment, U wave, QT interval changes and arrhythmias. They occur after head injury due to altered autonomic function and may not be associated with cardiac injury.

Premedication:

The same principles as those of craniotomy are applied.

Intraoperative and Postoperative Management:

The same principles as those of craniotomy are applied.

Anesthetic Management of Patients with Head Injury Undergoing Non-Neurologic Procedures

After even a mild head injury or after complete recovery from a moderate or severe head injury, the brain is abnormal and potentially vulnerable for **several weeks** at least.

During this period,

- Do only **the most emergent surgery** e.g., emergency laparotomy or thoracotomy to stop bleeding, and decrease the duration of surgery as much as possible (most orthopedic surgeries are not emergent).
- Take **the same precautions as in anesthetic management of head injury** such as maintaining CPP > 70 mm Hg, decreasing brain ischemia, and maintaining brain protection.

Anesthetic Management:

The same principles as those of head injury (especially ICP) (see before), in addition to:

1- Pupil Size Monitoring:

Pupil size can indicate the presence of **intra-cerebral hemorrhage** if both become **unequal.** It is not affected by anesthetic agents; therefore, during anesthesia of non-neurological procedures if the pupils become unequal, inform the surgeon to finish the surgery as soon as possible then do **neurological assessment and management**.

It is not a reliable sign for intra-cerebral hematoma because it is only **positive in < 50% of patients.**

2- The Choice of Regional Techniques for non-neurological procedures in head injured patients:

They have the following disadvantages:

a- **Epidural anesthesia:**

Due to the **large volume of anesthetic** solution used, **ICP** increases because CSF is shifted back to the intracranial compartment; so, it should be **avoided** and if used, the smallest volume of local anesthetics should be used and very slow injection should be done.

b- **Spinal anesthesia:**

It increases **the risk of tentorial herniation**. It is contraindicated in moderate and severe head injury. In mild head injury, it can be used only if CT scan is normal.

c- **Intravenous regional anesthesia (Bier's block) and orthopedic tourniquet:**

Release of the tourniquet (in lower limb>upper limb) can affect ICP in the following ways:

- It increases ICP.
- It causes unexpected fall in blood pressure due to sudden severe bleeding and blood shift.

Both decrease CPP.

Besides these disadvantages, the problem of **patient sedation during the regional techniques is added.** Therefore, **local nerve infiltration** is the safest technique used.

Anesthesia for Stereotactic Surgery and Neuro-Navigation

Definition: is the **use of imaging technology (CT scan/MRI)** and remote spatial orientation to guide slender devices for probing the brain and finding and resecting small lesions through small incisions.

A CT/MRI compatible stereo-tactic frame is applied to the head in stereo-taxis or to stickers in neuro-navigation.

Preoperative scans and rarely intraoperative MRI are used to determine the lesion's coordinates within the skull and to direct the localization of therapeutic probes, biopsy needles, endoscopes, resection devices....etc (figure 15-36).

Indications:

- Involuntary movement disorders.
- Intractable pain.
- Deeply situated brain tumors.
- Aneurysmal and vascular malformations.
- Epilepsy.

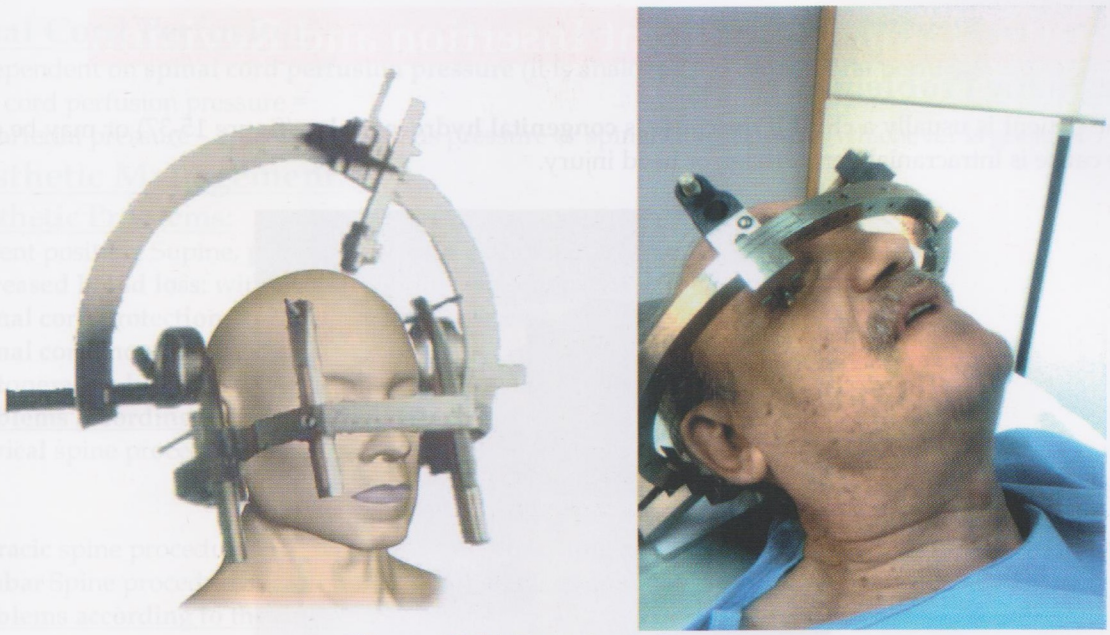


Figure 15-36: Stereotactic frames

Anesthetic Management:

Aim:

To **avoid any shift in the brain substances** that can be induced by an acute decrease in CBF or brain bulk as this results in **the biopsy needle missing its mark** in deep-seated lesions i.e., a resectable probe misses the bulk of a lesion **causing resection of normal functional brain tissue**.

Choice of Anesthesia:

a) Local Infiltration and Sedation:

It is the **most commonly** used to allow periodic evaluation of the patient.

Liberal use of local anesthetics decreases the hemodynamic effects of head pinning, frame and burr-hole placement.

Sedation is done by either:

- **Propofol infusion** that is of choice due to its negligible effects on CBF during normocapnia.

or • Very light **neurolept-analgesia** ± small increments of thiopentone in painful conditions.

b) General Anesthesia and Controlled Ventilation:

It is used for patients with **increased ICP and for pediatric patients**.

Induction:

Smooth induction with:

- **Local anesthesia infiltration** to decrease the hemodynamic effect of head pinning, frame and burr-hole placement.
- **Opioids that** are used to prevent hemodynamic effects of intubation, but once the dura has been entered, analgesic needs are negligible.
- **Intubation:** can be done easily, but the presence of the platform and the localizing frame may make **intubation difficult;** so, it is better to be performed either by awake or fiberoptic intubation.

Maintenance:

- **Normocarbia** is maintained, **but if inhalational** agents are to be used, **only mild hypocarbia ($PaCO_2$ around 35 mm Hg)** is induced to counteract anesthetic induced cerebral vasodilation.
- **Muscle relaxation: Complete paralysis** is needed to avoid the risk of coughing and cervical spine injury while the head is immobilized.

Intraoperative Problems:

- **Loss of CSF** from the incision may cause settling of brain contents and **shifting of intracranial lesions;** therefore, the burr-hole and the dural incision should be in a non-dependent position.
- The **repeated passage of probes and endoscopes** may initiate a process of **reactive brain edema** near the site of lesion resection causing increased ICP and postoperative coma. Therefore, delayed recovery should be investigated for the possibility of brain swelling and postoperative hematoma by CT scan, which may need emergency decompression surgery.

Anesthesia for CSF Shunt Insertion and Revision

Anesthetic Problems:

1- The patient is usually a **child** if the cause is **congenital hydrocephalus** (figure 15-37) or may be **elderly** if the cause is intracranial hemorrhage or head injury.



Figure 15-37: A child with congenital hydrocephalus

2- There is increased cerebrospinal fluid volume with enlarged ventricles, **causing a severe increase in ICP especially** in older children, which should be managed as before.

3- Types of hydrocephalus: it is either:

- Communicating (non-obstructive).
- Non-communicating (obstructive) due to congenital (e.g., Arnold-Chiari malformation), neoplastic, posttraumatic, or post-inflammatory lesions.

4- Abnormal enlargement of the head especially the frontal skull causing **difficult intubation.**

5- **Nerve compression** e.g. optic nerve and medullary nerves causing stridor, swallowing abnormalities, and tongue atrophy.

6- **Cardiovascular changes** include:

- With increased ICP, there is **systemic hypertension and bradycardia.**
- When the ventricle is drained, rapid **systemic hypotension** occurs which needs to be managed.

7- **Treatment is according to the type of the shunt:**

- **For ventriculo-peritoneal shunt:** The distal end of the shunt should be intra-peritoneal.
- **For ventriculo-atrial shunt** (to the right atrium): Observe the ECG during insertion for arrhythmias. Confirm the correct position of the distal end of the shunt by priming it with saline and aspirating blood. Thrombosis of internal jugular vein or superior vena cava, septicemia, meningitis, pleural effusion, pulmonary embolism, or pulmonary hypertension may occur.

Anesthesia for Pituitary Surgery (Hypophysectomy)

It is discussed in the chapter of "Endocrine Disease".

Anesthesia for Spinal Surgery

Spine surgeries include **spinal cord injury** or **spine (vertebrae) surgeries**. They are mainly for decompression of the spinal cord due to:

- Trauma for fixation of a spine (the most common).
- Tumor for resection.
- Degenerative diseases.
- Correction of deformity as scoliosis.
- Protrusion of an intervertebral disc for correction (laminectomy or discectomy).
- Protrusion of an osteophytic bone (spondylosis) for correction.
- Infection and abscess drainage.
- Vascular malformation.

Spinal Cord Perfusion:

It is dependent on **spinal cord perfusion pressure** (it is analogous to the cerebral perfusion pressure).
Spinal cord perfusion pressure =
Mean arterial pressure – spinal cord venous pressure or spinal CSF pressure (whichever is greater).

Anesthetic Management:

Anesthetic Problems:

1- Patient position: Supine, **prone and sitting** with their complications as **air embolism**.
2- **Increased blood loss**: with its precautions as elective hypotensive anesthesia.
3- **Spinal cord protection.**
4- **Spinal cord monitoring.**
5- **Postoperative blindness.**
6- **Problems according to the site of the procedure:**
- **Cervical** spine procedures: ▫ **Difficult intubation**: especially with neck stabilization.
  ▫ **Anterior approach** problems: pneumothorax and cardiovascular changes.
  ▫ **Postoperative edema** of the brain stem, neck, and airway.
- **Thoracic** spine procedures: ▫ Thoracotomy and **one lung anesthesia** are needed.
- **Lumbar** Spine procedures: ▫ **Regional anesthesia** e.g., spinal or epidural can be used.

7- **Problems according to the cause:**
- **Traumatic**: ▫ A, B, and C protocol.
  ▫ Acute spinal cord injury complications.
  ▫ Chronic spinal cord injury complications.
  ▫ Presence of associated injuries.
- **Ankylosing Spondylitis**, **rheumatoid Arthritis**, and **kyphoscoliosis** are discussed in the chapter of "Skin & Musculoskeletal Disease".
- Congenital abnormalities as **Down's syndrome:** is discussed in the chapter of "Pediatrics".

Preoperative Evaluation and Preparations:

1- Initial Resuscitation:

"**ABCDE" protocol** is important in traumatic spinal cord surgeries. "ABCDE" management is discussed above.

2- Airway Assessment: (especially in **cervical spine surgery**).

It should be assessed as follows:
- Assess **difficult intubation** such as mouth opening for tempro-mandibular joint, Mallampati classification…etc.
- Assess cervical spine instability. It is best to assume that an unstable cervical spine injury is present in any patient with head trauma until proved otherwise by radiography.

Both are discussed in full details in the chapter of "Airway Management".
- **Cervical immobilization** is indicated in cases of cervical instability. It is performed by one of the following methods:
  ▫ **Cervical collar** that is **not a totally effective** method to prevent cervical motion during direct laryngoscopy and it can **limit mouth opening**. It is used routinely (figure 15-38).



Figure 15-38: A cervical collar

▫ **Axial neck traction** that is **effective** and is used if definite injury is present, but it causes **difficult intubation** (figure 15-39).

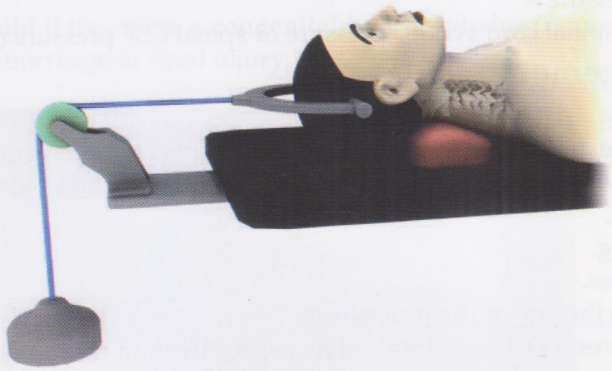


Figure 15-39: Axial neck traction

▫ **Complete halo-thoracic vest or halo-body fixation** that is the most effective and causes **impossible direct laryngoscopy** (figure 15-40).

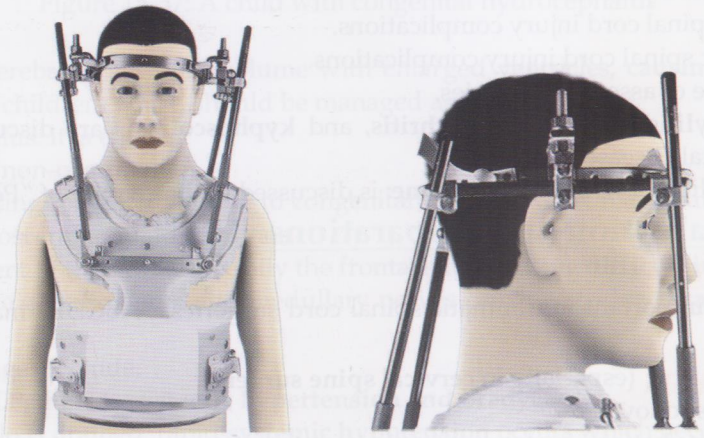


Figure 15-40: A complete halo-thoracic vest

• **Manual in-line stabilization**: The assistant's hands are placed on each side of the patient's face with the fingertips resting on the mastoid process with downward pressure against a firm table surface to hold the head immobile in a neutral position. This position is recommended in head trauma or cervical injury to help minimize cervical spine flexion and extension during direct laryngoscopy for tracheal intubation (figure 15-41).

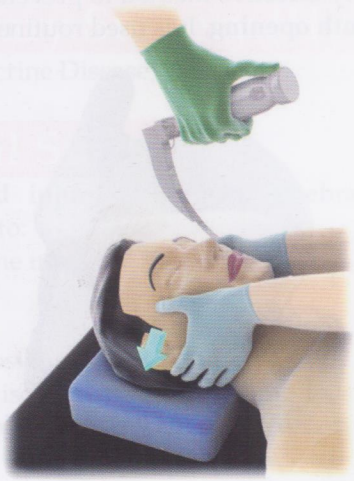


Figure 15-41: Manual in-line stabilization

- Conscious patients are instructed not to turn the head.
- **Cervical spine mobility and neck movement** should be carefully assessed.
- Radiology as x-ray, CT scan, and MRI are needed (see above with head injury).

3- Neurological Assessment: should be documented.

Assess the **motor and sensory deficits** as a baseline and at frequent intervals especially before and after patient transport and radiology.

4- Spinal Cord Protection: (to decrease neurological injury)

1- The best way to prevent further neurological injury to the spinal cord is **surgical decompression as soon as possible.**

2- Corticosteroids as **methyl prednisolone** is effective in prevention of further spinal cord injury if given within the first 8 hours after injury in a dose of 30 mg/kg i.v.

3- **Hypothermia:** Some authors advocate local hypothermia to the damaged area of the spinal cord to lessen further neurological injury.

4- **Ganglioside GM-1:** It helps axonal growth. A recent study has showed that it decreases neurological injury after ischemic insult.

5- **NMDA receptor antagonist:** GK-11 is tried.

5- Presence of Coexisting Diseases e.g., rheumatoid arthritis.

6- Drug Therapy.

7- Preoperative Investigations: are chosen according to the system affected:

- Respiratory investigations such as pulmonary function tests, arterial blood gases, and chest x-ray (e.g., if there is scoliosis affecting lung function).
- Cardiovascular investigations such as ECG, x-rays, echocardiography, and catheterization.
- Central nervous investigations such as myelogram and MRI (figure 15-42).

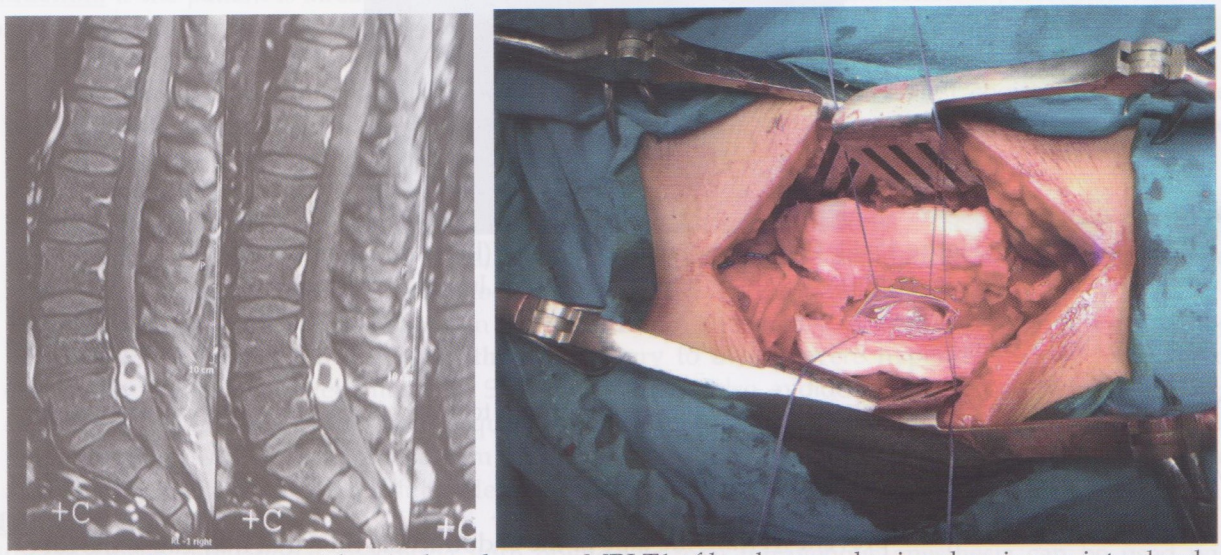


Figure 15-42: A patient with spinal cord tumor; MRI T1 of lumbo-sacral spine showing an intradural lesion opposite L4-L5 disc with areas of cystic changes.
The intraoperative image is during tumor excision

8- In Traumatic Spinal Injury: further examinations are required.

- Associated complications of acute spinal cord injury (see later) (figure 15-43 and 15-44).
- Associated complications of chronic spinal cord injury (see later).
- **Presence of Associated Injuries** such as tracheal, esophageal, and major vessels injury in penetrating cervical injuries, or thoraco-abdominal injuries.

9- Preoperative Patient Preparation:

1- **If intraoperative wake-up test** is planned, the patient should be informed and reassured that no pain or discomfort would be felt.

2- Management of any systemic disease that may be associated e.g., respiratory system with scoliosis……..etc.

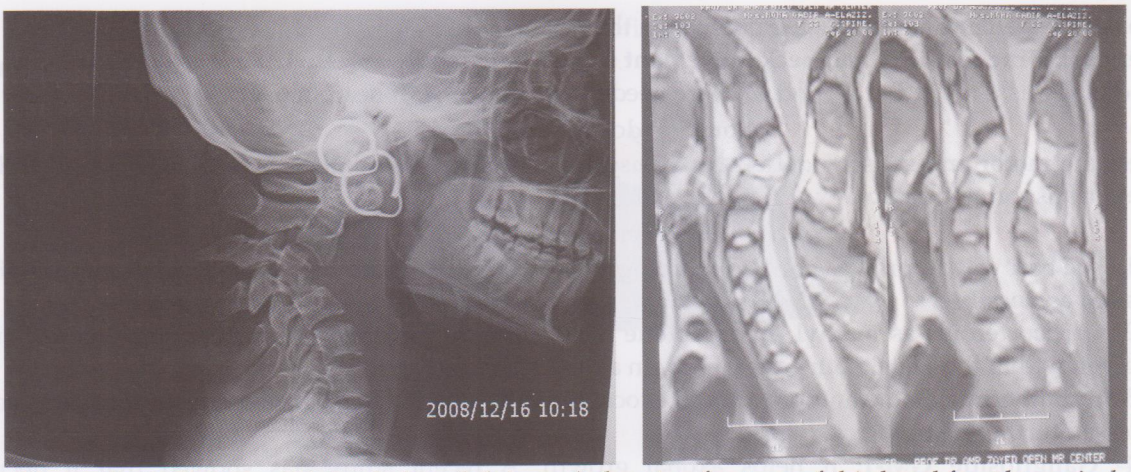


Figure 15-43: Plain x-ray lateral view (left image) showing fracture of third and fourth cervical vertebrae. MRI T2 (right image) of the same patient showing compressed, but intact, spinal cord at the level of the vertebral fractures

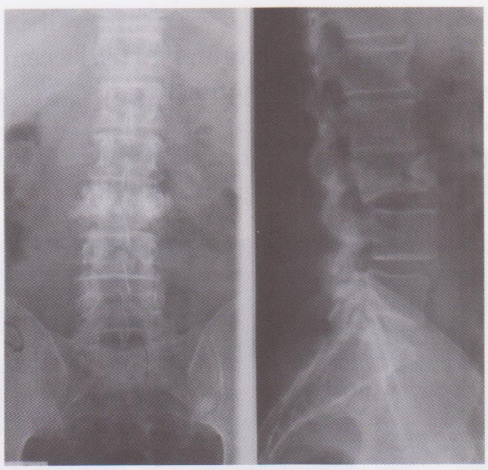


Figure 15-44: Plain x-ray antero-posterior (left) and lateral views (right) showing fracture of the third lumbar vertebra

Premedications:

1- Sedatives:

Avoid heavy sedation in patients with respiratory impairment to avoid further respiratory depression.

2- Anticholinergics:

Value: • To treat bradyarrhythmias.

• Anti-sialagogue to ▫ facilitate fiberoptic bronchoscopy.

▫ prevent wetting the tape of the endotracheal tube that may cause the tube to slip especially that the patient is in the prone position.

3- Opioids:

It is important if patients are in severe pain e.g., degenerative diseases.
It should be avoided if there is respiratory depression.

4- Protection against aspiration:

- H_2 receptor blockers to decrease gastric secretions.
- Metoclopramide to increase gastrointestinal motility.

Intraoperative Management:

Monitoring:

Besides the standard monitors, the following monitors may be added.

- **Spinal cord monitoring such as wake up test, somato-sensory evoked potentials (SSEPs) and motor evoked potentials.**
- **Electromyography:** Muscle relaxants should be avoided. It is the most sensitive test in spine surgery. It is indicated when nerve roots are at risk during the procedure.

- **Temperature monitoring**.
- **Venous air embolism monitoring** such as esophageal stethoscope, transesophageal echocardiography.
- Invasive blood pressure especially if controlled hypotensive anesthesia is indicated and to obtain arterial blood gases.
- Left ventricular dysfunction monitoring such as central venous pressure, pulmonary artery pressure …etc.
- Urine output as it is a lengthy operation.

Position:

1- Supine position: for anterior thoracic fusion by trans-thoracic approach, and anterior approach for cervical spine surgery.
2- Sitting position: for posterior approach for cervical spine surgery.
3- Prone position: for posterior approach for cervical spine surgery, and thoraco-lumbar spine surgery.
Techniques, contraindications, and complications are discussed before in chapter "Respiratory Disease".

Choice of Anesthesia

A) Regional Anesthesia:

Epidural and spinal anesthesia can be used in some cases such as **lumbar** discectomy.
Advantages:
- It decreases blood loss.
- It decreases nausea and vomiting.
- It decreases incidence of deep venous thrombosis.
- It decreases early postoperative pain.

B) General Anesthesia:

Induction: If the patient is already not intubated, **rapid sequence crash induction** is performed with the following precautions:
- Care for cervical instability.
- Precautions for difficult intubation. Awake fiberoptic intubation is the first choice in cooperative patients with unstable cervical spine. Methods of difficult intubation are discussed in details in the chapter of "Airway Management".
- **Induction agents:**
  Etomidate is of choice because it produces minimal cardiovascular effects.
  Thiopentone or propofol can be used, but large doses should be avoided because they accentuate hypotension in patients with spinal shock in case of spinal cord trauma.
- **Succinylcholine** can be **used** safely in the **1st 24 hours** after injury. It should be **avoided** in periods **between 1 – 2 days up to 6 – 8 months after injury** to avoid severe hyperkalemia (K^+ is released excessively from denervated muscles). Succinylcholine is also avoided if malignant hyperthermia is suspected e.g., in scoliosis. If rapid sequence induction with succinylcholine is considered essential, precurarization with 5-10 mg atracurium can be used and methods of treating hyperkalemia should be available such as Ca^{++}, $HCO3^-$, insulin/dextrose …etc.

Maintenance:
Either balanced inhalational anesthesia with opioids or total intravenous anesthesia can be used with muscle relaxants and controlled ventilation.
Inhalational Agents:
Sevoflurane and desflurane are preferred to the older agents because they allow **faster recovery** which is necessary for:
- **Intraoperative wake up technique** to test motor function.
- **Postoperative early neurological assessment.**

Disadvantages of potent volatile agents:
- They interfere with monitoring of SSEPs and wake-up test.
- They produce dose-dependent myocardial depression.

Opioids: Advantages:
- They do not interfere with monitoring of SSEPs.
- They provide stable depth of anesthesia.
- They provide rapid and pain free recovery during wake-up test.

Total Intravenous Anesthesia: is suitable because it allows faster recovery especially if SSEPs are monitored.

Muscle relaxants:

Pancuronium is used if there is bradycardia e.g., during spinal cord injury.

Intermediate acting muscle relaxants are preferred to allow rapid recovery during wake up test without the need for a reversal.

Intraoperative Fluid Therapy:

Proper replacement by isotonic crystalloid solutions (and blood if needed) should be guided by central venous pressure and pulmonary artery pressure with **avoiding:**

- **Circulatory under-load** to avoid severe hypotension in patients with spinal shock or hemorrhagic shock.
- **Circulatory over-load** to avoid pulmonary edema in patients with left ventricular dysfunction.

Avoid glucose containing solutions because hyperglycemia worsens ischemic neurological injury.

Spinal cord surgeries are procedures associated with massive blood loss in most cases; therefore, methods decreasing blood loss should be maintained such as preoperative autologous donation...etc.

Intraoperative Problems:

1- Venous Air Embolism: especially in sitting position.

2- Respiratory Dysfunction in cases of traumatic spinal cord injuries due to:

- injury of motor fibers supplying intercostals or diaphragm (at C3-5 level).
- edema of the spinal cord that can produce dysfunction in several dermatomes above the actual surgical site.

3- Intraoperative Hypothermia is a common problem due to large wound size, prolonged surgeries, and loss of thermal regulation in acute spinal cord injury.

4- Increased Blood Loss: is a common problem; therefore, the following methods are important:

- **Preoperative autologous donation** and hemodilution.
- **Elective hypotension**.
- Wound infiltration by a weak epinephrine solution.
- Red blood cell **salvage device** should be used.
- The site of the wound should be elevated e.g., prone position with avoiding increase in the intra-abdominal pressure.

5- Problems with Anterior Cervical Approach: Care should be taken for:

- Injury of the trachea, lung (pneumothorax), esophagus, sympathetic chain, carotid sheath or sinus (causing cardiovascular changes).
- Injury of the recurrent laryngeal nerve that can be diagnosed intraoperatively by electromyographic testing of vocal cord function using special endotracheal tubes with built in electrode wires (electro-myographic tubes or EMG tubes) (figure 15-45).

6- Problems with Transthoracic Approach:

It needs thoracotomy and one lung anesthesia.

7- Spinal Cord Protection: such as corticosteroids and intentional hypothermia.



Figure 15-45: An EMG tube

8- If abnormal SSEPs are detected intraoperatively during fixation of spinal cord injury showing signs of ischemia such as: • Decreased amplitude > 50%.
• Increased latency > 50%.
• Complete loss of waveform.

Then: • Adequate oxygenation should be maintained.
• $PaCO_2$ should be normalized if the patient is hyperventilated.
• Arterial blood pressure should be normalized if controlled hypotension was used, or slightly increased above the normal to improve spinal cord perfusion.
• Hypovolemia or anemia should be corrected.
• Inform the surgeon to search for surgical causes and correct it immediately e.g., too much traction or pressure by instrumentation.
• If abnormal SSEPs persist, do wake-up test to determine whether the instrument needs to be adjusted or removed.

Extubation:

Awake extubation should be applied with possibility of re-intubation.

Postoperative Management:

Postoperative Analgesia:

• In thoracic or lumbar spine surgery, postoperative epidural analgesia is very effective. Generally the epidural catheter is placed by the surgeon in the operative field.
• Opioids are used with caution.

Postoperative Complications:

1- Postoperative Edema: is either:

a- Brainstem Edema: occurs after procedures in the cervical region due to edema of the cervical cord after surgery which may extend upward along the spinal cord to affect:
• **The respiratory center** resulting in gradual respiratory insufficiency if the patient has been extubated and in breathing spontaneously.
• **Cranial nerve IX and X** resulting in difficulty in coughing and swallowing.

Therefore, close monitoring for respiration and ability to cough and swallow is done postoperatively.

Management:
• Decrease postoperative cervical cord edema by corticosteroids and mannitol.
• If respiration is affected (clinically or by arterial blood gases), re-intubation is required.

Usually postoperative edema subsides within 48 – 72 hours.

b- Neck and Airway Edema: occurs after procedures in the cervical region.

Risk factors of postoperative edema after procedures in the cervical region include:
• Surgery > 10 hours.
• Obesity.
• Re-operation.
• Surgery of ≥ 4 cervical spine levels.
• Surgery involving C2.
• Surgery needing > 4 units blood.

2- Postoperative Blindness:

Spinal surgeries in prone position and with excessive blood loss are risk factors for postoperative blindness.

Pathophysiology, risk factors, clinical pictures, prevention and treatment are discussed in the chapter of "Miscellaneous Problems in Anesthesia & Intensive Care".

3- Respiratory Care: especially if the respiration is affected preoperatively e.g., with scoliosis in the form of: • Deep breathing exercise.
• Incentive spirometry.
• Bronchodilators, analgesics, and mucolytics.
• Adequate hydration.
• Postoperative ventilation that may be needed.

4- Neurological Complications: such as paraplegia.

Special Conditions Affecting the Spine

1- Traumatic Spinal Cord Injury:

A) Acute Spinal Cord Injury:

Trauma is the most common cause of acute spinal cord injury e.g., head trauma, penetrating injury in proximity, crush injuries… etc. The most common site of injury is **C_{5-6} and T_{12}- L_1**.

Although the spinal cord is not usually anatomically transected, complete or nearly complete neuronal dysfunction may occur below an affected dermatomal level. Thus from a functional standpoint, the spinal cord may appear transected.

Physiological Sequelae of Acute Spinal Cord Injury: depend on the level of the lesion:

High lesions produce the most severe damage which includes:

1- Respiratory Dysfunction:

a- **Respiratory Impairment** due to:

- **Intercostal muscle paralysis** if the lesion is at C_5 (the diaphragm is intact). These patients have a vital capacity around 25% of the normal resulting in respiratory impairment especially on exercise or stress. Recruitment of accessory muscles is necessary to improve respiratory capacity. This may take up to 6 months.
- **Diaphragmatic paralysis** if the lesion is above C_3 (the diaphragm is innervated by the phrenic nerve C_3-C_5). This abolishes the diaphragmatic ventilation and makes artificial ventilation mandatory.

b- Paralysis of intercostal and abdominal muscles creates **ineffective cough** and decreases **chest wall compliance** with tidal volume at or near the closing capacity with tendency of airway closure. This causes retention of secretions, atelectasis, ventilation/perfusion mismatching, and intrapulmonary shunting (figure 15-46).

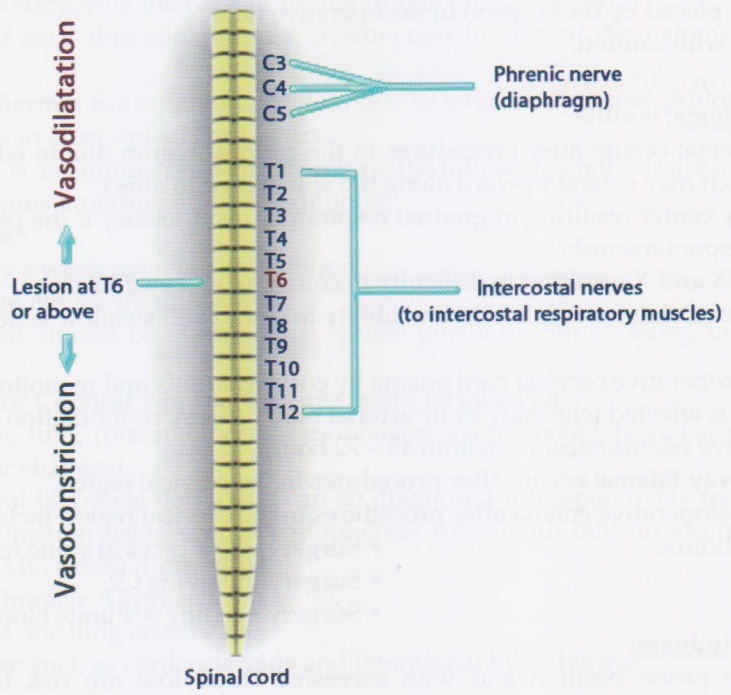


Figure 15-46: Spinal cord trauma

2- Cardiovascular Dysfunction:

a- Spinal Shock (Neurogenic Shock):

There are losses of

- **Sympathetic outflow (i.e., sympathectomy)** due to interruption of sympathetic fibers that are descending to the T_1-L_2 spinal cord segments and causes hypotension, bradycardia, and hypothermia. **Priapism** may occur in males owing to unopposed parasympathetic action.
- **Spinal reflexes (i.e., areflexia).**
- **Sensation.**
- **Motor power (i.e. flaccid paralysis).**

These effects occur below the level of spinal cord injury. These losses last from **hours to days, to even weeks (typically 1-3 weeks)** then reflexes gradually return, sympathetic over-activity, muscle spasm and spasticity gradually occur.

b- Brady-Dysrhythmias:
They range from sinus bradycardia to profound brady-dysrhythmias up to cardiac arrest which can occur any time from hours to days after injury. It occurs due to loss of the T1-T4 sympathetic innervation of the heart and is enhanced by hypoxia.
Compensatory tachycardia does not occur because sympathetic reflexes are absent (the only autonomic reflex present is the vagal reflex which can produce dangerous levels of bradycardia).
c- Left Ventricular Dysfunction:
It can occur even in young, previously healthy individuals due to decreased sympathetic outflow and increased vagal tone. This causes depression of myocardial contractility, so on increasing circulatory blood volume, pulmonary edema can occur easily.

3- Autonomic Dysfunction:

a- Loss of Thermal Regulation: below the level of injury.
Body temperature will equilibrate with room temperature (i.e., poikilothermy) causing either:
- Hypothermia, especially in the air-conditioned intensive care unit, that may mask a febrile response.

or • Hyperthermia.

b- Gastrointestinal Dysfunction:
Gastric atony, dilatation, hyper-secretion, delayed emptying and paralytic ileus which increase the risk of aspiration are common.
c- Bladder Dysfunction.

4- Sensory and Motor Deficits:

Lesions above C_7 and T_1 cause **quadriplegia**, while lesions above L_4 cause **paraplegia.**
After upper motor neuron denervation, avoid suxamethonium administration from 1-2 days post-trauma up to 6-8 months due to severe hyperkalemia produced.

B) Chronic Spinal Cord Injury

Physiological sequelae:

In **addition to** the physiological sequelae that occur **with acute spinal cord injury**, the following dysfunctions may also occur.

1- Respiratory Dysfunction:

- **Pulmonary emboli** due to immobility (with increased incidence of deep venous thrombosis). Compression stockings are usually indicated. Some centers warfarinize tetraplegics 5 days after initial presentation.
- **Pulmonary infections** and **upper airway obstruction** due to inability to cough and clear secretions.
- **Dyspnea** due to airway hyperactivity.
- Some patients need **partial ventilatory support and diaphragmatic pacing**.

2- Cardiovascular Dysfunction:

- **Reduced blood volume** (up to 60 mL/kg, a reduction of approximately 20%).
- **Abnormal response to the Valsalva maneuver** with continued drop in blood pressure (no plateau) and lack of overshoot with release of pressure.
- **Profound postural hypotension** with gradual improvement after initial injury (never back to normal).

3- Autonomic Dysfunction: It appears after resolution of spinal shock.

Autonomic Hyperreflexia or Dysreflexia (Mass Reflex):

Causes:

- It occurs due to **loss of normal descending cortical inhibitory impulses**; therefore, cutaneous stimuli such as bladder or rectal stimulation; surgery, or visceral stimulation below the level of injury can produce intense autonomic sympathetic reflexes. This is associated with extremely exaggerated involuntary movement.
- 85% of patients with **lesions at T6 or above** show **autonomic hyperreflexia** because this will completely isolate the splanchnic nerves from higher centers of control, whereas lesions to lumbar levels of the cord will result in a grossly intact peripheral sympathetic nervous system supplying the splanchnic nerves.

Autonomic hyperreflexia is **unlikely to occur** with spinal cord transection **below T10** (because the splanchnic bed is still innervated and able to vasodilate which prevents hypertension from developing). and unlikely to occurs **after 9 months of injury**.

Stimuli to Levels Below the Site of Spinal Cord Injury:

- Urological stimulus: such as bladder distension, catheter insertion…etc.
- Obstetric stimulus: such as labor, cervical dilation…etc.

- Bowel obstruction/fecal impaction.
- Acute abdomen.
- Fractures.
- Surgical incisions.
- Rarely minor trauma to skin or cutaneous infection such as bedsores.

Response:

One of the above stimuli causes:

- **Severe vasoconstriction below** the spinal cord lesion resulting in severe **life threatening hypertension** leading to headache, blurred vision, cerebral hemorrhage, myocardial infarction and even left ventricular dysfunction and pulmonary edema with reflex bradycardia due to carotid sinus stimulation.
- **Severe cutaneous vasodilatation above** the spinal cord lesion resulting in facial flushing, sweating, seizures, dysrhythmias, hypothermia, nasal stiffness, penile erection, Horner's syndrome (sometimes), and even loss of consciousness.

Treatment:

Patients with negative history for this reflex are still at risk for its occurrence during surgery due to the intense stimulus that surgery provides.

1- Immediate withdrawal of the initial reflex trigger is of choice.

2- Vasodilators such as Na nitroprusside and nifedipine and sympathetic blockers such as clonidine or phentolamine to treat hypertension.

3- Good deep general, regional, or local anesthesia can prevent this reflex.

N.B.: Blocking afferent pathways with topical local anesthetics applied to the urethra, as for a cystoscopic procedure, often does not prevent autonomic hyperreflexia as this form of anesthesia does not block the bladder muscle proprioceptors which are stimulated on bladder distension. Autonomic hyperreflexia may first manifest postoperatively when the effects of the anesthetic drugs begin to wane.

4- Electrolyte Imbalance:

1- **Hypercalcemia** due to immobilization resulting in:
- Dysrhythmia.
- Osteoporosis.
- Renal stones and infections which lead to renal failure.

2- **Acute hyperkalemia** from 1 -2 days up to 6 – 8 months after injury, by succinylcholine administration.

5- Poor Peripheral Perfusion resulting in:

- **Decubitus Ulcers (Bedsores):** that easily progress to systemic sepsis and septicemia.
- **Difficult venous access.**

6- Pancreatitis and Cholecystitis are common.

7- Anemia: usually mild unless associated with chronic illness such as decubitus ulcers.

8- Dys-Endocrine Syndrome: There are usually
- Abnormal glucose tolerance due to insulin resistance.
- Decreased HDL-cholesterol level.

9- Chronic Pain, Depression, Skeletal Muscle Spasticity and Contractures:

It is also called; sympathetic meditative pain, chronic nerve pain, central pain, phantom pain, neuropathic pain, dys-esthetic pain, and central dys-esthetic syndrome.

Cause:
- Loss of downstream inhibition.
- Release of excitatory pathways.
- Stimulation of secondary nociceptive pathways.
- Alignment of structural and synaptic connection.
- Re-growth of neurons at the area of injury.

It is characterized by: paroxysmal pain super-imposed on background constant aching or dys-esthetic pain. Spasticity may be triggered by minor trauma such as light touch. It may be violent enough to injure the patient and may be severe enough to interfere with surgery and physiotherapy.

Treatment:

1- Drugs: amitriptyline, carbamazepine, intrathecal analgesics.

2- Dorsal column stimulation.

3- Surgical ablation of dorsal roots of spinal cord.

4- **Baclofen (oral or intrathecal pump)** for disabling spasticity. Intrathecal baclofen can cause rhabdomyolysis and renal dysfunction on acute withdrawal.
More details of chronic pain management are discussed in the chapter of "Pain Management".

10- Syringomyelia:

It can occur **several years** after injury resulting in increased pain and neurological deficits. It is treated by a diverting shunt between the syrinx and subarachnoid space.

Spinal Cord Injury with Pregnancy

Anesthetic Problems and Precautions:

1- Cardiovascular problems: There are **exaggerated postural hypotension** and **worsened response to caval occlusion.**
2- Respiratory problems: Respiratory reserve is reduced with **increased risk of respiratory failure and pneumonia**.
3- Labor (even without pain) is a potent cause of **autonomic hyperreflexia** in those with lesions above T5-6 (autonomic hyperreflexia may be the first sign of labor in such patients); therefore, **adequate analgesia and anesthesia** during labor is essential to avoid **autonomic dysreflexia (not only to relive pain)**. Epidural anesthesia may be less effective than spinal anesthesia in preventing autonomic hyperreflexia due to relative sparing of the sacral segment with the epidural technique.
Labor pain will not be felt in complete lesions above T5, while patients with lesions between T5 and T10 will be aware of some contractions.
4- Spinal injury increases the incidence of **preterm labor**. The risk increases with higher level injury.
5- Due to physiological changes of pregnancy such as increased blood volume and decreased functional residual capacity, patients with high level quadriplegia will need **elective controlled mechanical ventilation** especially at the late weeks of pregnancy.

2- Endoscopic Spine Surgery

Advantages:
- It decreases postoperative pain.
- It decreases blood loss.
- It decreases pulmonary complications.
- It decreases intensive care utilization.

Technique:

a- **Cervical Spine**:
It is **rarely** done by endoscopic surgery. It needs **sitting position** (with its complications).

b- **Thoracic Spine**:
It needs **thoracoscopy and one lung ventilation**.

c- **Lumbar Spine**:
It is **an anterior laparoscopic lumbar spine procedure** with the following precautions:
- It is similar to any laparoscopic procedure with **CO_2 insufflation with all its risks**.
- **Excessive bleeding** due to **possible injury of inferior vena cave**.
- It may be done **under local anesthesia and sedation** if posterior endoscopic discectomies done.

3- Ankylosing Spondylitis

4- Rheumatoid Arthritis

5- Kyphoscoliosis

They are discussed in the chapter of "Skin & Musculoskeletal Diseases".

6- Congenital Abnormalities such as Down's Syndrome

It is discussed in "Pediatrics".

Cervical Spine

Anatomy:

The neck is divided into 2 portions:

I) The Upper (or Atlanto-Axial) C Spine:

It includes:

1- C_1 (the Atlas):

C_1 is **a ring** with large superior and inferior articular surfaces which interact with the skull base above and C_2 below respectively. It has no body or spinous process. There are no intervertebral discs between occiput and C_1 or between C_1 and C_2.

2- C_2 (the Axis):

It is the most unusual. It has a long, thumb-like extension of the vertebral body, which extends upward to pass via the anterior arch of C_1. It is called the **dens or the odontoid process** which can be considered embryologically as the body of C_1 (figure 15-47).

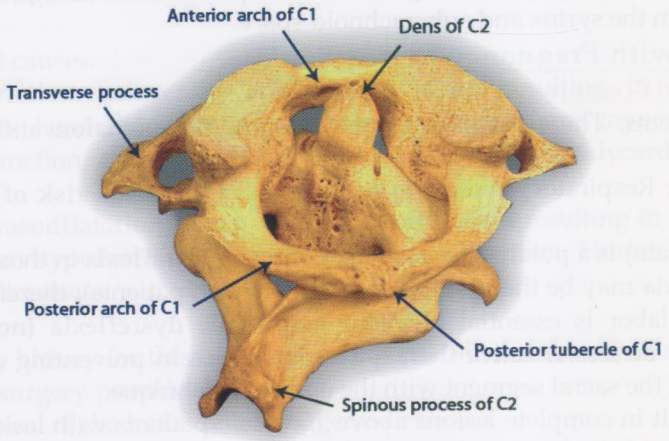


Figure 15-47: The Atlas (C1) and Axis (C2) with slight rotation

The anterior atlanto-dental interval **(AADI)** is the space between the anterior aspect of the odontoid and the back of the anterior arch of C_1.

The posterior atlanto-dental interval **(PADI)** is the space between the posterior aspect of the odontoid and the anterior aspect of the posterior arch of C_1. The spinal cord passes via PADI.

N.B.: C_1 is a rigid ring; so, if the AADI gets larger, the PADI must get smaller.

II) The Sub-Axial Spine (Below The Axis of C_2):

The vertebrae C_3 to C_7 are similar to normal vertebrae; having a body, lamina, spinous process, and transverse process. The anterior tubercle of the transverse process of C_6 is known as **Chassaignac's tubercle.** The spinous process of C_7 (known as the **vertebra Prominens**) is the most easily palpated one.

Motion (Biomechanics):

Three motions of the neck are present in a normal middle aged person.

a- **Flexion/Extension** (max down to max up): It ranges from **130-140** degrees of arc.

b- **Lateral Bending** (shoulder to shoulder): It ranges from **85-90** degrees of arc.

c- **Axial Rotation** (max left to max right): It ranges from **160-170** degrees of arc.

There is some reduction in motion with age. For every decade of life after the age of 30 years, there is about a 10 degrees loss in the range of flexion and extension of the cervical spine.

These movements are produced by the following joints:

1- Occipito-C_1 Joint:

Ligaments are tight and allow little motions as:
- Minimal lateral bending (5-10 degrees).
- Minimal flexion (only 5 degrees).
- Minimal extension (only 20 degrees).
- Minimal axial rotation.

All are measured from the neutral position.

2- C_1-C_2 Joint:

Great rotation is produced with the odontoid process as the pivot point. Flexion and extension are about 10 degrees of each from the neutral position.

N.B.: Patients with an O-C_2 fusion cannot rotate their neck well.

3- C_2-C_3 and Below Joints:

The movement is more uniformly distributed where maximal motion occurs at C_4-C_5-C_6; so, these are the most common sites of injury.

Lateral bending (head on shoulder) is roughly 5-10 degrees/segment below C_2.

Vertebral Ligaments:

They are either:
- Active Ligaments which are constantly under tension.

- Passive Ligaments which are under tension only at the extremes of the range of motion of the cervical spine.

Stability Structures:

They are either:

- The flexion-stability structures consisting of the tectorial membrane and the posterior longitudinal ligament.
- The extension-stability structures consisting of the ligamentum flavum, the tectorial membrane, the anterior longitudinal ligament, and the anterior atlanto-occipital membrane.

N.B.: After injury or with normal aging, these ligaments can be calcified resulting in limitation of motion of the cervical spine.

Motion with Intubation:

During laryngoscopy, the laryngoscope is primarily applied with an upward lift (and a little bit of angular force, even if we do tell people not to do this). This force can be as high as 50-70 N (40 N is enough to lift 10 Ibs).

Greater force is used in difficult laryngoscopies which cause:

- Near maximal extension of O-C_1.
- Flexion below C_2-C_3.

Therefore, any intervention that impedes this motion (upper extension and lower flexion) leads to more difficulty in visualizing the glottis e.g.,

- Surgical O-C_1-C_2 posterior fusion that results in very difficult direct laryngoscopy.
- External stabilization methods (traction, manual stabilization, collars….etc.).
- Surgical fusion (anterior or posterior) for more than two or three levels below C2 that results in some difficulty, but fusion of one or two levels does not affect intubation.

Therefore, you cannot stabilize the neck without impending the laryngeal view.

Q: Discuss management of cervical spine injury?

A: At first discuss anatomy and motion of cervical spine.

Then discuss anesthetic management as above.

Anesthesia for Neurosurgery in Infants and Children

Physiology of Central Nervous System in Infants and Children

The same physiology **as that of adults** with the following **differences**:

- The limits of **cerebral autoregulation** may be shifted to significantly lower values i.e., mean arterial pressure **20-60 mm Hg**. The margin of safety is narrower as the infant is less well to compensate for acute hypo-or hypertension. Low mean arterial pressure increases the risk of ischemia while hypertension in infants may increase the risk of intracranial hemorrhage.
- Hyperventilation i.e., **low $PaCO_2$ in infants** produces **brisk cerebral vasoconstriction** with a risk of **inducing cerebral ischemia** especially when $PaCO_2$ is < 20 mm Hg.

Clinical Picture of Increased ICP in Neonates and Infants

- The **typical clinical picture** of increased ICP such as bradycardia, elevated blood pressure, dilation of the pupils and papilloedema is usually **not present** early in the course of the disease because the infant skull is not fully ossified and is more compliant than the adult skull; therefore, the cranium can substantially expand causing **hydrocephalus** before producing clinical attention.
- The **signs and symptoms** of increased ICP appear **late in the course of the disease**.
- Increased head circumference, bulging fontanelles, widened cranial sutures "sundowning" of the eyes, irritability, lethargy, poor feeding, or lower motor deficits are common.

Anesthetic Management

The same anesthetic principles **as these of adult**, but with the following differences:

- **The blood volume** may be **contracted** because of poor intake or recurrent vomiting.
- Airway assessment should be performed because of possibility of difficult intubation with hydrocephalus.
- Premedication is usually performed by **oral midazolam** (intranasal or i.v. can be used) because it produces neither respiratory depression nor changes in $PaCO_2$ with doses up to 0.7 mg/kg with a maximum of 20 mg.

• **Induction:**

- **Inhalational induction** (in an uncooperative child) via a face mask is usually used. All volatile anesthetics cause an increase in CBF. The anesthesiologist should control ventilation as soon as possible and mildly hyperventilate the patient to decrease $PaCO_2$ to offset the rise in CBF until an i.v. access is established.
- **I.v. induction** by propofol or thiopentone is preferable (in a cooperative child) because:
  - I.v. agents (except ketamine) decrease ICP.
  - This technique avoids airway complications such as laryngospasm/bronchospasm as both increase $PaCO_2$ and thus elevate CBF and ICP.

Common Neurosurgical Procedures in Pediatrics

1- Pediatric Brain Tumors:

2/3 of childhood brain tumors are located infratentorially and may need sitting craniotomy.

2- Vascular Malformation:

It is common in children.

3- Anti-Epilepsy Surgery:

It includes surgical resection of a seizure focus or placement of vagal nerve stimulator. It has the following anesthetic problems:

- There is possibility of perioperative seizures.
- Altered drug metabolism due to induction of liver enzymes with anticonvulsant therapy.
- Awake craniotomy is preferred as it allows the patient to respond to commands while the specific brain area to be excised is identified, but in young children this procedure is not practical due to lack of cooperation.

4- Traumatic Brain Injury:

It can occur even in low velocity trauma that can cause severe brain insult due to:

- the larger surface area of the pediatric head.
- the weaker neck musculature.

5- Craniosynostosis and Cranio-Facial Reconstruction

Craniosynostosis is a condition that occurs due to premature closure of one or more cranial sutures (the most common is the sagittal suture). It causes deformity of the skull needing craniectomy to avoid brain atrophy from the increased intracranial tension (figure 15-48).



Figure 15-48: Plain x-ray of the skull of a patient with craniosynostosis showing copper-beaten appearance indicating increased intracranial tension

Types:
- Scaphocephaly: early fusion the sagittal suture.
- Anterior plagiocephaly: early fusion of 1 coronal suture.
- Brachycephaly: early bilateral coronal suture fusion.
- Posterior plagiocephaly: early closure of 1 lambdoid suture.
- Trigonocephaly: early fusion of the metopic suture (figure 15-49 and figure 15-50)

Anesthetic Problems:
- Difficult airway management that may even require tracheostomy to secure airway.

- Exophthalmos and optic atrophy.
- Increased intracranial pressure and hydrocephalus.
- Seizures.
- Mental retardation.
- Congenital heart disease.



Figure 15-49: Carpenter syndrome with craniosynostosis

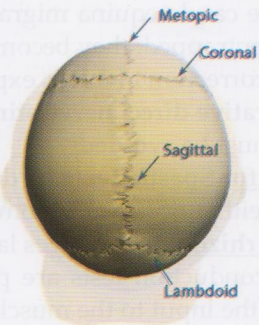


Figure 15-50: The normal sutures of the skull

6- Dysraphism:

It is incomplete closure of the raphe (dysraphism) during fetal development allowing neural herniation, which persists after birth. It is either:

a- Encephalocele: It is a herniation of the cranial contents (with dura and cerebrospinal fluid) out of the skull through a defect. It may be obvious or may occur intranasally (difficult to be detected).

b- Meningocele and Myelomeningocele:

They occur due to failure of closure of the caudal end of the neural tube.

- Meningocele is a sac that contains meninges.
- Myelomeningocele is a sac that contains meninges and neural elements causing various degrees of motor and sensory defects e.g., flaccid paralysis (figure 15-51).

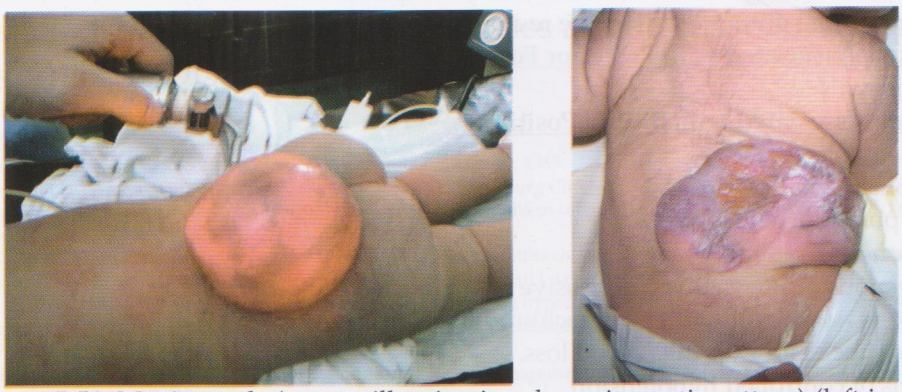


Figure 15-51: Meningocele (a trans-illumination shows its cystic pattern) (left image) and myelomeningocele (right image)

Anesthetic Problems:

- **Motor and sensory deficits** may be present, but suxamethonium does not produce abnormal release of K^+.
- As it is in the back, **awake intubation** is done while the child is **in the lateral position** to avoid pressure on the sac; then surgery is done while the child is in prone position.
- **Cerebrospinal fluid leakage** may occur, leading to **volume and electrolyte disturbances**.
- **Latex allergy** is a common association with neural tube defects.
- Associated congenital anomalies:
  - **Dislocated hip and club foot** (needing surgical correction).
  - **Extrophy of bladder** (needing surgical correction).
  - **Hydrocephalus.**
  - **Congenital heart disease.**
  - **Gastro-esophageal reflux** causing **aspiration.**

7- Hydrocephalus:

See above.

8- Spinal Cord Surgeries:

a- Surgery for Tethered Cord Syndrome:

• Tethered cord syndrome results from developmental anomalies which **entrap** the nerves of **the cauda equina**. The cauda equina migrates rostrally with normal growth from the position of L4 to L1-2. If the nerves are entrapped, they become stretched and create **neurological deficits.**

• Surgical correction involves exposure of the cauda equina and release of the tethering anomalies.

• **Intraoperative direct nerve stimulation** is utilized to guide release of the tethered cord and thus **muscle relaxants** must be **avoided**.

b- Surgery for Spasticity: (e.g., due to cerebral palsy)

It involves either dorsal rhizotomy or placement of a baclofen pump.

Dorsal rhizotomy involves laminectomy in the prone position where specific nerves are targeted after nerve conduction tests are performed intraoperatively. Then selected nerve roots are transected to relieve the input to the muscles and decrease the contracture with the following precautions:

- Neuromuscular blocking agents are contraindicated.
- Precautions of the prone position.
- Severe postoperative pain requiring analgesia.
- Postoperative spasticity requiring benzodiazepines.

Intrathecal baclofen infusion: is discussed in the chapter of "Pain Management".

Complications in Neuroanesthesia

Every complication should be diagnosed by history and investigations and managed.

A) Complications Associated with Brain Protective Measures:

• Side effects of mannitol and diuretics.
• Side effects of subarachnoid drainage.

B) Complications Associated with Craniotomy:

• Excessive sedation during awake craniotomy may compromise the airway.
• Increased intracranial pressure may cause re-intubation postoperatively.

C) Complications Associated with Posterior Fossa Craniotomy:

• Brainstem injury.
• **Complications Associated with Sitting Position:**
  ▫ Venous air embolism.
  ▫ Pneumocephalus.
  ▫ Postural hypotension.
  ▫ Hypertension due to pins.
  ▫ Impeding venous drainage due to excessive neck flexion.

D) Complications Associated with Subarachnoid Hemorrhage:

• Hypovolemic shock and excessive blood loss.
• Complications of controlled hypotension.
• Complications of Temporary Clip Occlusion (Aneurysmal Trapping).
• Intraoperative rupture of cerebral aneurysm.
• Delayed recovery e.g., due to a cerebrovascular stroke
• Cerebral vasospasm and side effects of triple H therapy.
• Hydrocephalus.
• Cerebral Salt Wasting Syndrome.
• Neurogenic Pulmonary Edema.
• Increased ICP.
• Deep Venous Thrombosis and Pulmonary Embolism.

E) Complications during Interventional Neurosurgery:

1- Complications of radiographic contrast agents such as allergy.
2- Exposure to radiations.
3- Anticoagulation to prevent thrombo-embolic complications e.g., i.v. heparin and complications of heparin such as thrombocytopenia.
4- Acute arterial occlusion or vasospasm.

5- Risk of deliberate hypotension if used.
6- Risk of acute subarachnoid hemorrhage during coiling of the aneurysm.
7- Complications of Triple H therapy to treat cerebral vasospasm.
8- During obliteration of arterio-venous malformation by cyano-acrylate glues which cause permanent closure of the abnormal vessels by embolization. Passage of glue into a draining vein can result in acute hemorrhage in younger patients and pulmonary embolism.

F) Complications Associated with Head Trauma:

- Cervical Spine injury with difficult and dangerous intubation.
- Diabetes insipidus.
- Post-traumatic seizures.
- Electrolyte disturbances.

G) Complications Associated with Trans-Sphenoidal Hypophysectomy

- Difficult intubation with Acromegaly.
- Injury to surrounding structures during surgery such as optic chiasma.
- Endocrinal disturbances such as hypo- or hyper-thyroidism.
- Infections.

H) Complications Associated with Spinal Surgery:

- Complications of sitting position such as air embolism, or of prone position such as glottic edema and difficulty of re-intubations.
- Hypovolemic shock and excessive blood loss.
- Affection of somato-sensory evoked potentials by N_2O and volatile agents.
- Hypothermia (intentional or unintentional).
- Postoperative blindness.
- Problems with cervical spine procedures: ▫ Difficult intubation and in-line stabilization.
  ▫ Pneumothorax with anterior approach.
  ▫ Postoperative edema of the brainstem, neck, and airway.
- Problems with thoracic spine procedures: ▫ Complications of one lung anesthesia.
- Complications due to spinal cord injury (acute and chronic).

Other neurological and psychiatric diseases are discussed in chapter "Neuro-psychiatric Diseases".

Further readings:

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Web sites:

- http://www.nice.org.uk/Guidance/CG56/Guidance/pdf/English
- http://emedicine.medscape.com/article/1175957-overview

RENAL DISEASES

16

• Renal physiology • Effects of anesthesia on renal function • Effect of renal disease on pharmacokinetics of drugs • Evaluation of renal function	• Anesthesia for patient with renal impairment or failure; acute and chronic • Perioperative and intensive care oliguria • Renal replacement therapy • Plasma exchange

Renal Physiology

Renal Circulation

Renal function is intimately related to renal blood flow; therefore; the kidneys are the only organs for which O_2 consumption is determined by the blood flow. The reverse is true in other organs.

Blood flow to both kidneys is 20-25% of cardiac output.

Blood Supply of the Kidneys

The blood supply to the kidney passes through the following sequence of arteries:

The **aorta**, a **single renal artery** to each kidney in the renal pelvis, **interlobar arteries** at the junction between renal cortex and medulla, **arcuate arteries**, **interlobular arteries**, **afferent arteriole** (each nephron is supplied by a single afferent arteriole), network of **glomerular capillaries** which drain in a **single efferent arteriole**, **peri-tubular capillary (pars recta)** (around proximal tubules), **vasa recta** (around the loop of Henle), **venules**, **interlobar veins**, and finally **a single renal vein** from each kidney which drains into the **inferior vena cava** (figure 16-1).

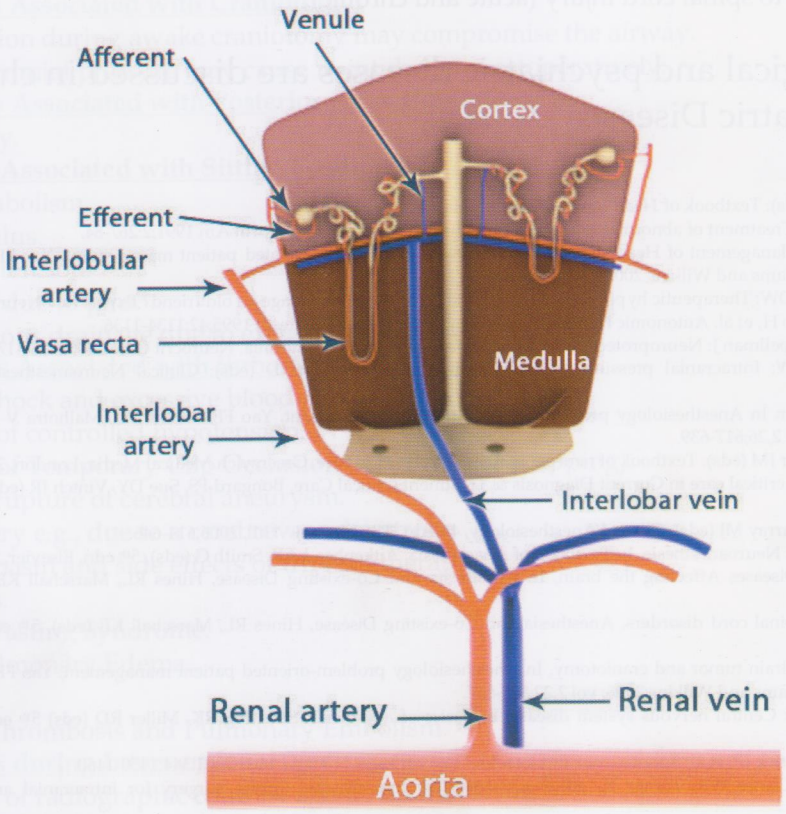


Figure 16-1: Blood supply of the kidneys

Renal Plasma Flow (RPF)

It is measured by **the Fick's principle** using **para-amino-hippuric acid (PAH) clearance**. PAH is **completely cleared** in one passage via the kidneys because:
- It is **filtered** by the glomerulus.
- It is **secreted** by the renal tubule.

$$\text{RPF} = \text{clearance of PAH} = \frac{U_{PAH} \times V}{RA_{PAH} \quad RV_{PAH}}$$

$$\text{As } RV_{PAH} \text{ is negligible, so} = \frac{U_{PAH} \times V}{RA_{PAH}} = \frac{U_{PAH} \times V}{P_{PAH}} = 660 \text{ mL/min}$$

Where U_{PAH} = Urine concentration of PAH in mg/mL.
RA_{PAH} = Renal artery concentration of PAH in mg/mL.
RV_{PAH} = Renal vein concentration of PAH in mg/mL.
P_{PAH} = plasma concentration of PAH in mg/mL.
V = Urine volume in mL/min.

N.B.: Actually, as only 90% of PAH is excreted by the human kidney; therefore, the clearance of PAH (C_{PAH}) underestimates RPF by approximately 10%. To improve the accuracy, RPF can be estimated from the disappearance curve of intravenously injected ^{131}I-labelled PAH, eliminating the potential error introduced by timed urine collection.

N.B.: Renal circulation differs from other circulations in:
1- Mean glomerular capillary pressure is maintained at 45 mm Hg (it is 25 mm Hg in other capillary networks) due to presence of a 2nd resistance vessel which is the efferent arteriole. This favors glomerular filtration.
2- Mean peri-tubular capillary pressure (in pars recta) is only 15 mm Hg and lower than intra-tubular pressure. This favors tubular reabsorption.

Renal Blood Flow (RBF)

$$\text{RBF} = \frac{\text{RPF}}{1 \quad \text{hematocrit}} = 1200 \text{ mL/min.}$$

Control of RBF:

I) Intrinsic Control:

Autoregulation (in the cortex not in the medulla) maintains RBF normally in the range **80-180 mm Hg** mean blood pressure. This may be due to an intrinsic myogenic response of afferent arterioles. Outside the autoregulation limits, RBF (and glomerular filtration rate) becomes pressure-dependent. Glomerular filtration stops when mean blood pressure is < 40-50 mm Hg.

II) Extrinsic Control:

A-Vasoconstrictors:

They are the **salt retaining systems**. They protect against
- hypovolemia,
- hypotension, and
- hyponatremia.

They include:

1- Sympatho-Adrenal System:

- **Adrenal catecholamines** (epinephrine and norepinephrine) cause:
  - Direct vasoconstriction of afferent arterioles.
  - Stimulation of renin-angiotensin system.

Therefore, the net effect is relative preservation of glomerular filtration rate (GFR).

- **Sympathetic nervous system:** (T_4-L_2 via celiac and renal plexuses).
  β_1 (in juxta-glomerular apparatus) produces stress induced vasoconstriction causing decreased RBF.
  α_1 (in renal vasculature) produces:
  - stress induced vasoconstriction causing decreased RBF
  - an increase in Na^+ reabsorption in proximal tubules.

  α_2 decreases Na^+ reabsorption (resulting in an increase in Na^+ and water excretion).

2- Renin-Angiotensin-Aldosterone System:

• **Angiotensin II:** Decreased afferent arteriolar pressure stimulates renin release which increases angiotensin II levels. The latter produces generalized vasoconstriction which decreases RBF (both afferent and efferent arterioles are constricted, but because the efferent arteriole is smaller, its resistance becomes greater than that of afferent arteriole); therefore, the net effect is relative preservation of glomerular filtration rate (GFR).

Preservation of GFR by angiotensin II is mediated by prostaglandin synthesis. It is blocked by inhibitors of prostaglandin synthesis such as non-steroidal anti-inflammatory drugs.

• **Aldosterone** causes preservation of GFR i.e., water and Na^+ retention.

N.B.: **Tubulo-Glomerular Balance and Feedback:**

Changes in **renal tubular flow rates affect the GFR** as an **increase in tubular flow results in decreased GFR** while a decrease in tubular flow results in increased GFR. This feedback plays an important role in maintaining GFR constant over a wide range of perfusion pressures. The exact mechanism is not clear, but the macula densa may induce reflex changes in the afferent arteriole and possibly glomerular capillary permeability. **The increase in tubular flow stimulates the macula densa** (containing chemo-receptors) which elevates **angiotensin II levels.** The latter produces **afferent arteriolar vasoconstriction** resulting in **decreased GFR and vice versa.**

Local release of **adenosine** (in response to volume expansion) may inhibit renin release resulting in afferent arteriolar dilatation.

The phenomenon of pressure natriuresis (i.e., decreased Na^+ reabsorption in response to increased arterial blood pressure) may be due to this tubulo-glomerular balance (see later).

3- Arginine Vasopressin (AVP) (Anti-Diuretic Hormone):

AVP acts on two types of receptors:

- **V1 receptors** that cause vasoconstriction of afferent arterioles resulting in decreasing GFR.
- **V2 receptors** that cause water reabsorption by collecting ducts which results in concentrating urine.

4- Endothelin:

It is an endothelial derived vasoconstrictor factor. It plays a major role after endothelial injury.

5- Serotonin: It decreases RBF.

B-Vasodilators:

They are the **salt excreting systems**. They protect against
- hypervolemia,
- hypertension, and
- hypernatremia.

They include:

1- Prostaglandins (PGs):

PG D_2, PG E_2, and PG I_2 cause renal vasodilation.

2- Atrial Natriuretic Peptide (ANP):

It is produced due to atrial stretch. It causes:

- vasodilation of afferent and vasoconstriction of efferent arterioles resulting in increased GFR.
- a decrease in Na^+ reabsorption in proximal and collecting tubules.

Both cause diuresis.

3- Nitric Oxide:

It is an endothelial derived vasodilator factor. It plays a major role after endothelial injury.

4- Dopamine:

It acts on two receptors:

- Renal D_1 receptors (in low doses): It dilates afferent and efferent arterioles and decreases reabsorption of Na^+ in proximal tubules.
- Presynaptic D_2 receptors on postganglionic neurons: It inhibits neuronal release of norepinephrine.

Distribution of RBF

Normally 80% of RBF goes to cortical nephrons (with short loops of Henle) and 15% of RBF goes to juxta-medullary nephrons (with long loops of Henle). The RBF is very low in the inner medulla which is important for the counter-current mechanism.

Redistribution of RBF away from cortical to juxta-medullary nephrons (i.e., direction of RBF to the medulla) occurs in the following conditions:

- sympathetic stimulation e.g., heart failure and stress.
- an increase in catecholamines and angiotensin II.

The significance of this redistribution is controversial, but it is associated with Na^+ retention.

The glomerulus

Each kidney is made up of about 1 million functional units called nephrons. There are 2 types of nephrons:

a- Cortical nephrons (85%): They lie in the cortex and have short loops of Henle (lacking a thin ascending part of loop) which dip only into the outer medulla.

b- Juxta-medullary nephrons (15%): They lie in juxta-medullary area of the cortex and have long loops of Henle which dip into the inner medulla (figure 16-2 and 16-3).

The glomerulus is composed of tufts of capillaries that jut into Bowman's capsule. Endothelial cells in the glomeruli are separated from the epithelial cells of Bowman's capsule only by their fused basement membrane. The endothelial cells are perforated with relatively large fenestrae (70-100 nm), while the epithelial cells are perforated with small fenestrae (25 nm) i.e., they are tight together.

Glomerular filtrate requires passage via 3 layers which are size-selective and charge-selective:

1- The fenestrated capillary endothelium (which restricts the passage of cells only).
2- The basement membrane (which restricts passage of plasma proteins).
3- The epithelial podocytes.

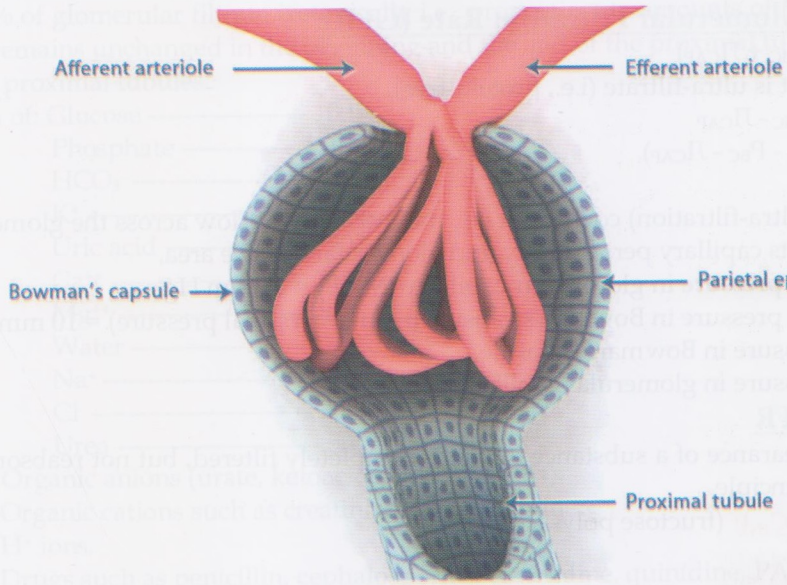


Figure 16-2: The glomerulus

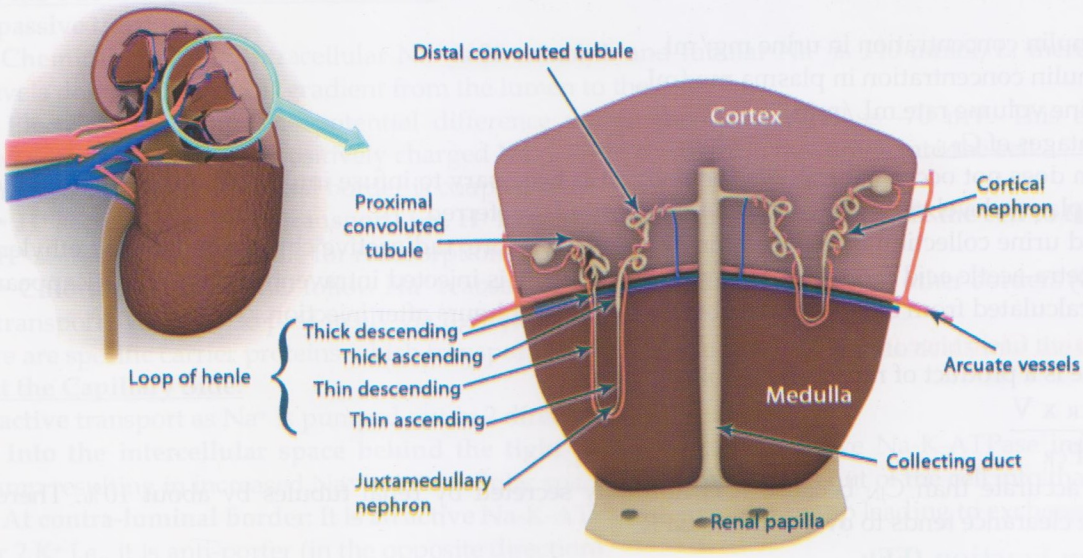


Figure 16-3: Cortical and juxtamedullary nephrons

Glomerular Filtration

It is normally **20% of RPF**. It allows **180 liters/day (125 mL/min)** of fluid and solutes to pass through the glomerular capillaries. The fluid which enters the proximal tubule from the Bowman's space is an ultrafiltrate of plasma i.e., it is virtually protein-free.

Factors Affecting Filtration of Solutes via Glomerular Basement Membrane:

1- Molecular Weight (M.W.):

The lower the molecular weight the easier the filtration i.e., increased molecular weight decreases filtration of substances. **At M.W. ≥ 70 000 Dalton, no filtration** occurs. The M.W. of the albumin is 69 000; so, only small amount can pass.

2- Molecular Charge:

The glomerular basement membrane consists mainly of **negatively charged** sialo-proteins. It repels the negatively charged ions and **attracts the positively and neutrally charged** particles (the M.W. of dextran is similar to some proteins, but dextran is 10-20% more filterable because it has no charges while proteins are negatively charged).

3- Molecular Shape:

It may facilitate passage of some molecules. Albumin has a tapering shape which facilitates its passage.

Factors Affecting Glomerular Filtration Rate (GFR):

$GFR \alpha (P_{CAP} + \Pi_{BC}) - (P_{BC} + \Pi_{CAP})$

As Π_{BC} is negligible as it is ultra-filtrate (i.e., protein-free),

$GFR \alpha P_{CAP} - P_{BC} - \Pi_{CAP}$

$GFR = K_F (P_{CAP} - P_{BC} - \Pi_{CAP})$

Where:

K_F = The slaving (ultra-filtration) coefficient i.e., the resistance to flow across the glomerular basement membrane. It reflects capillary permeability and glomerular surface area.

P_{CAP} = Hydrostatic pressure in glomerular capillary (MAP) = 45 mm Hg.

P_{BC} = Hydrostatic pressure in Bowman's capsule (renal interstitial pressure) = 10 mm Hg.

Π_{BC} = Oncotic pressure in Bowman's capsule.

Π_{CAP} = Oncotic pressure in glomerular capillary = 25 mm Hg.

Measurement of GFR

GFR is measured by clearance of a substance which is completely filtered, but not reabsorbed or secreted depending on Fick's principle.

a- Clearance of Inulin (C_{IN}): (fructose polysaccharide)

$$C_{IN} = \frac{U_{IN} \times V}{P_{IN}}$$

= GFR = 125 (± 25) mL/min in man.

Or = 95 (± 20) mL/min in woman.

Where:

U_{IN} = Inulin concentration in urine mg/mL.

P_{IN} = Inulin concentration in plasma mg/mL.

V = Urine volume rate mL/min.

Disadvantages of C_{IN}:

- Inulin does not occur naturally in the body. It is necessary to infuse inulin intravenously to achieve a steady plasma level; therefore, creatinine clearance is preferred.
- Timed urine collection is required for 24 hours; therefore, radioactive chromium-labelled ethylene di-amine tetra-acetic acid (^{51}Cr-EDTA) can be used, which is injected intravenously and the disappearance rate is calculated from blood sample obtained at 2 and 4 hours after injection.

b- Creatinine Clearance (C_{CR}):

Creatinine is a product of muscle metabolism.

$$C_{CR} = \frac{U_{CR} \times V}{P_{CR}}$$

It is less accurate than C_{IN} because it is normally secreted by renal tubules by about 10%. Therefore, creatinine clearance tends to overestimate GFR.

Filtration Fraction (FF):

It is the ratio of GFR to RPF.

$$FF = \frac{GFR}{RPF} = \frac{C_{IN}}{C_{PAH}} = \frac{120}{600} = 0.2\ (20\%)$$

GFR is dependant on the relative tones of both the afferent and efferent arterioles. Vasodilation of afferent arterioles or vasoconstriction of efferent arterioles increases GFR and FF.

Tubular Function

The role of the renal tubule is:

1- To **modify** the volume and composition of the glomerular filtrate according to the needs of the organisms. So, the GFR (180 L/day) is reduced by 99% to 1.8 L/day (urine volume/day).

2- To **conserve** filtered substances which are essential for maintenance of homeostasis such as glucose, HCO_3...etc.

3- To **excrete** waste products of ingestion or metabolism e.g., K^+, urea, creatinine...etc.

4- To **regulate** acid base status.

5- To **concentrate or dilute** the urine according to the body need.

A) The Proximal Tubule:

It reabsorbs **70%** of glomerular filtrate isotonically i.e., proportionate amounts of Na^+ and H_2O; therefore, the osmolality remains unchanged in the beginning and the end of the proximal tubule (290 mOsmol/kg).

The function of proximal tubules:

a- Reabsorption of: Glucose ---------- 100%
Phosphate ---------- 100%
HCO_3^- ---------- 90%
K^+ ---------- 90%
Uric acid ---------- 90%
Ca^{++} ---------- 90%
Mg^{++} ---------- 90%
Water ---------- 70%
Na^+ ---------- 70%
Cl^- ---------- 70%
Urea ---------- 50%

b- Secretion of: Organic anions (urate, ketoacids, and bile salts).
Organic cations such as creatinine and dopamine.
H^+ ions.
Drugs such as penicillin, cephalosporins, cimetidine, quinidine, PAH, and diuretics.

c- Production of ammonia.

I- Na^+ Reabsorption:

a- At the Tubular Side (Luminal Border):

It is **passive** transport.

1- Chemical gradient: Intracellular Na^+ is 30 mmol/L and tubular Na^+ is 140 mmol/L; therefore, Na^+ travels down the chemical gradient from the lumen to the cell.

2- Electrical gradient: The potential difference within the tubular cell is -70 mV. This creates an electrical gradient for the positively charged Na^+ ions to travel from the lumen into the cell.

Na^+ reabsorption at the luminal border is coupled with

- **H^+ secretion (counter-transport) i.e., H^+ moves opposite the Na^+ from inside the cell to the lumen.** H^+ secretion is responsible for reabsorption of 90% of HCO_3^- (see later).
- **Chloride (Cl^-) and H_2O** follow Na^+ reabsorption at the luminal border and other borders (Co-transport). Cl^- can also pass freely via tight junction.

There are specific carrier proteins which transport phosphate, glucose, and amino acids into the cell.

b- At the Capillary Side:

It is **active** transport as Na^+ is pumped out in 2 directions (figure 16-4):

1- Into the intercellular space behind the tight junction: It is an active Na-K-ATPase independent pump resulting in increased Na^+ in intercellular space. H_2O and Cl^- pass out of the cell into that space.

2- At contra-luminal border: It is an active Na-K-ATPase dependant pump leading to exchange of 3 Na^+ for 2 K^+ i.e., it is anti-porter (in the opposite direction).

K^+ is freely permeable via the cell membrane and may diffuse passively out again into peri-tubular space. Na^+ is reabsorbed into peri-tubular capillary. Net loss of intracellular positive charges favors absorption of other cations (K^+, Ca^{++}, and Mg^{++}). Therefore, Na-K-ATPase provides the energy for the reabsorption of most solutes.

There is active K^+-Cl^- co-transport (symporter i.e., in the same direction) that extrudes both ions at the capillary side of cell.

c- Movement of Na^+, Cl^- and H_2O into the peri-tubular capillary is governed by starling's forces.

The driving forces are • hydrostatic pressure of the peri-tubular space (small).
• oncotic pressure of the peri-tubular capillary (the main controlling factor).

The opposing forces are: • hydrostatic pressure of the peri-tubular capillary.
• oncotic pressure of the peri-tubular space (negligible).

Control of Na^+ reabsorption is discussed in full details in chapter "Fluid & Electrolyte Disturbances".

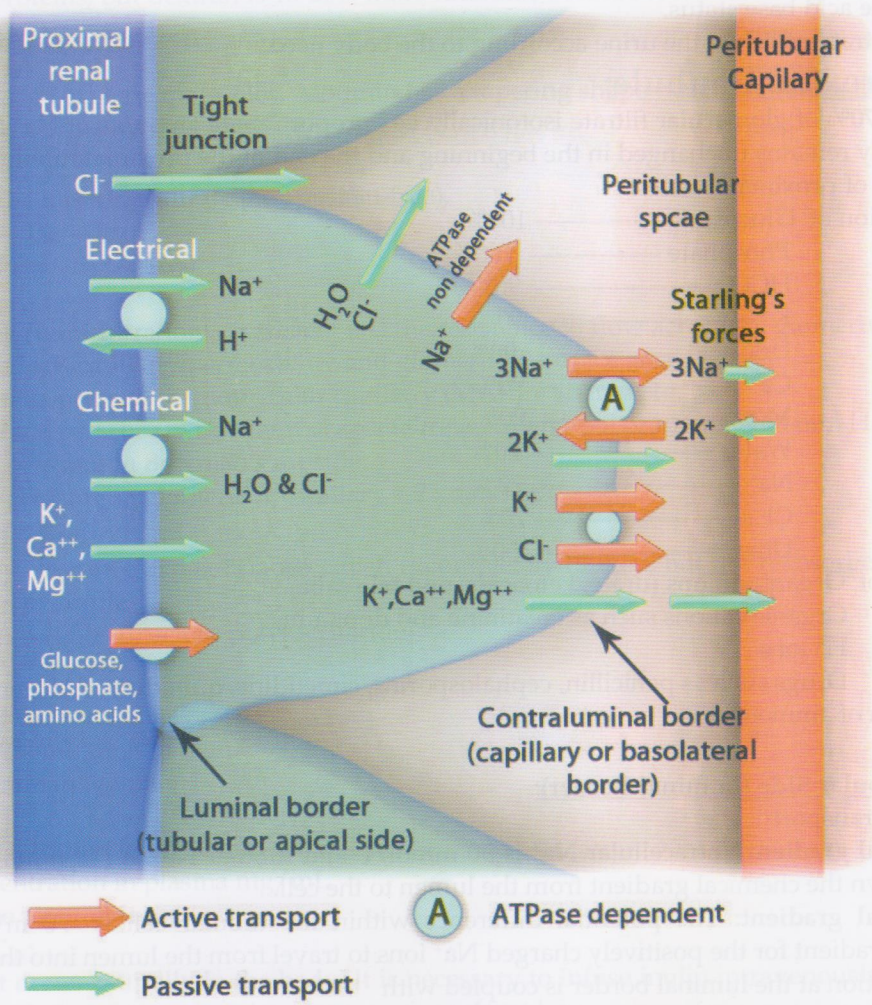


Figure 16-4: The proximal tubules

II- Rate-Limited Tubular Transport:

Rate-limited tubular transport mechanism is applied for transport of glucose 100%, phosphate 100%, amino acids 100%, HCO_3^- 90% and sulphate. When the plasma concentration of a substance (e.g., glucose) increases, the tubular reabsorption of glucose is increased until a plateau is reached where no further increase in glucose reabsorption can occur (figure 16-5).

At this point, the transport mechanisms are saturated. At such plasma concentration (renal threshold) glucose starts to appear in urine. Glucose excretion increases in parallel with the filtered load of glucose as the plasma glucose concentration increases (renal threshold for glucose = 10 mmol/L in man). The plateau at which maximal glucose reabsorption occurs is called the **tubular maximal reabsorption** for glucose

(Tmg). The point at which glucose reabsorption reaches its maximum is not a fine cut-off, but a small curve called **splay**. It is caused by the **heterogenecity of the nephron** population in respect to glucose reabsorption. **Some nephrons reabsorb glucose maximally at a lower plasma glucose** concentration **than other nephrons** within the kidney. A large splay is the cause of one type of renal glucosuria.

Tm_g = 20 mmol/min.
Tm_{HCO3^-} = 3 – 3.5 mmol/min.
$Tm_{phosphate}$ = 0.125 mmol/min

The glucose, phosphate, amino acids, and HCO_3^- share a co-transport system with Na^+; as when proximal tubular reabsorption of Na^+ decreases, Tm is also decreased for them.

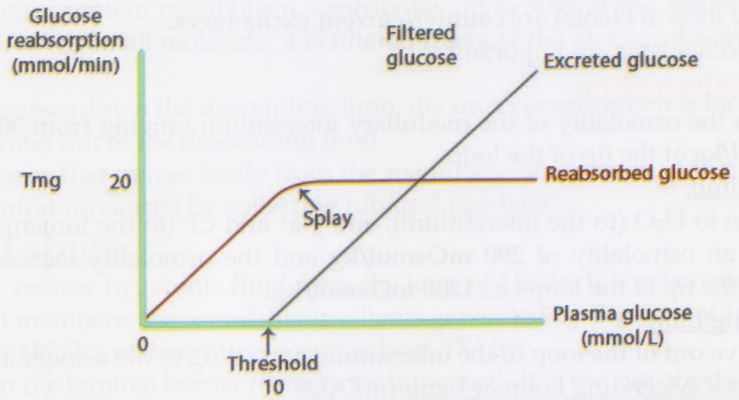


Figure 16-5: Glucose reabsorption

III- Bicarbonate Transport:

It is important in renal regulation of acid-base balance. Bicarbonates enter the tubular lumen as $NaHCO_3$ that dissociates into HCO_3^- (a relatively impermeable anion) and Na^+. The Na^+ passes into the cell in exchange for H^+ ions. The H^+ ions combine with HCO_3^- in the tubular lumen to form carbonic acid. The enzyme carbonic anhydrase (CA) present on the brush border of the proximal tubular cell splits carbonic acid into CO_2 and H_2O. Both of which are freely permeable and enter the tubular cell. The intracellular CA enzyme reforms carbonic acid which in turn dissociates into H^+ and HCO_3^- ions. HCO_3^- passes via the basal border into the peri-tubular space and is available for reabsorption by the peri-tubular capillary. H^+ ions can be extruded to the tubular lumen in exchange for Na^+ and the cycle is repeated (figure 16-6).

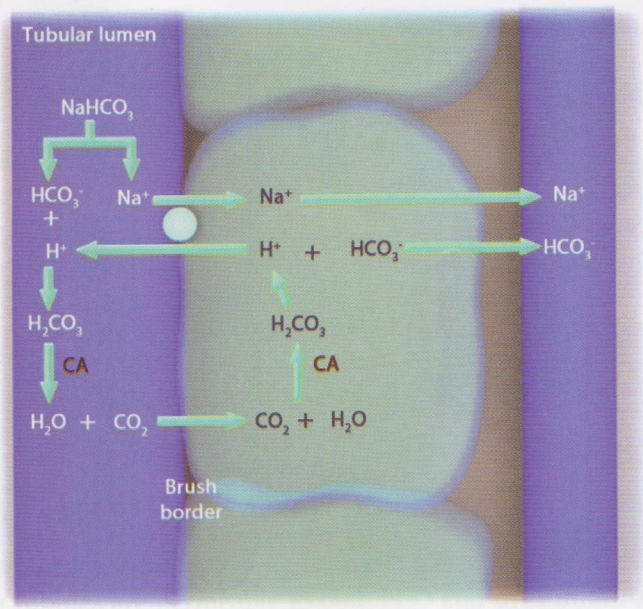


Figure 16-6: Bicarbonate transport

B) The Loop of Henle:

It absorbs **15-20%** of glomerular filtrate (H_2O, Na^+, Cl^-, K^+, Ca^{++}, and Mg^{++}).

The loops of Henle of the juxta-medullary nephrons are important. Each consists of:

- a thin descending limb.
- a thin ascending part.
- a thick ascending part. It is either medullary (medullary thick ascending loop or limb "mTAL") or cortical.

The tubular fluid enters the loop with an osmolality of 290 mOsmol/kg and leaves it at 100 mOsmol/kg.

Counter-Current Mechanism

The loop of Henle is the active part. It is a **counter-current multiplier**.

The vasa recta (around loop of Henle) are **counter-current exchangers**.

Two main transport mechanisms are important.

1- Na^+ and H_2O Reabsorption:

There is an increase in the osmolality of the medullary interstitium ranging **from 300 mOsmol/kg** in the cortex to **1200 mOsmol/kg** at the tip of the loop.

a- The Descending Limb:

It is freely permeable to H_2O (to the interstitium), and Na^+ and Cl^- (to the lumen). The fluid enters the descending limb at an osmolality of **290 mOsmol/kg** and the osmolality increases slowly until it is equivalent to that at the tip of the loop i.e., **1200 mOsmol/kg.**

b- The Thin Ascending Limb:

Both Na^+ and Cl^- move out of the loop to the interstitium according to the osmolality gradient.

c- The Medullary Thick Ascending Loop or Limb (mTAL):

It is **impermeable to water**, but Na^+, Cl^-, and K^+ move to the interstitium by an active transport process (mainly Cl^- is transported actively and Na^+ is co-transported with Cl^-). This is responsible for the gradual increase in medullary interstitial osmolality. Ca^{++} and Mg^{++} reabsorption occur at the thick ascending limb. Parathyroid hormone stimulates Ca^{++} reabsorption. The mTAL is the major site of action of **loop diuretics** that inhibit Na-Cl reabsorption in mTAL.

d- The Cortical Thick Ascending Limb:

The filtrate fluid enters the cortical thick ascending limb with osmolality of 300 mOsmol/kg and then the osmolarity decreases where the filtrate fluid enters the distal convoluted tubules with osmolality of 100 mOsmol/kg (figure 16-7).

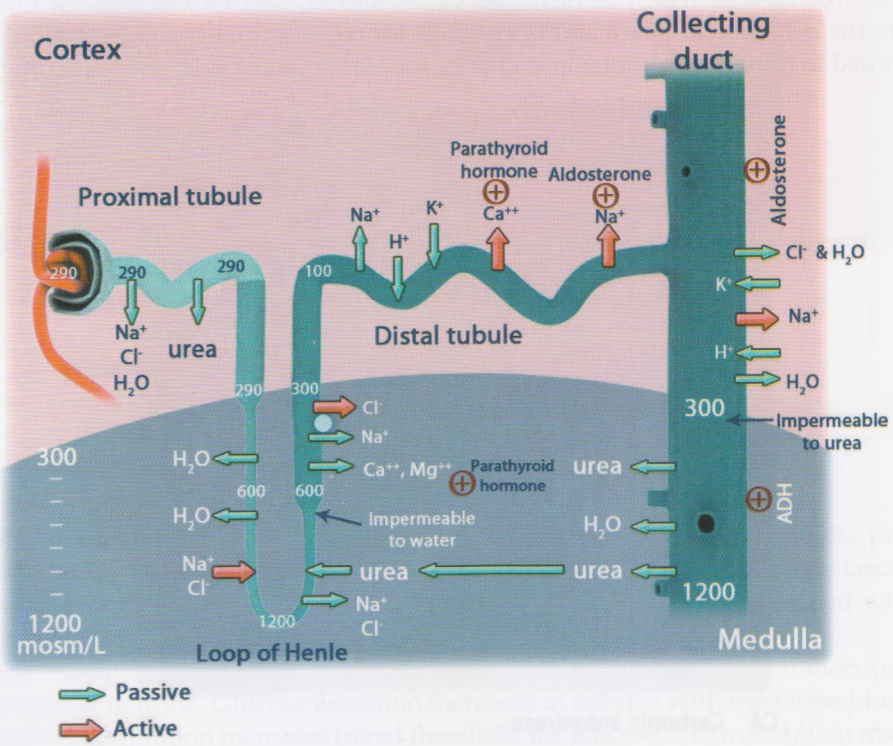


Figure 16-7: Loop of Henle

The Vasa Recta:

- H_2O and solutes move freely (no active transport) across it.
- The osmolality of blood entering the vasa recta is the same as that of the fluid entering the descending limb i.e. 290 mOsmol/kg. As it passes down to the tip of the loop, the osmolality gradually increases to 1200 mOsmol/kg. This is achieved by the passage of H_2O and solutes across its surface.
- The blood flow is significantly slower in the lower parts of the vasa recta to improve the efficiency of this exchange.
- As the vasa recta move from the medullary tip back towards the cortex, the same process occurs and the osmolality returns to 290 mOsmol/kg.

2- Urea Recycling:

Urea, a waste product of protein metabolism, contributes up to **50% of the osmolality of the medullary interstitium.** Because it is a small molecule, it is filtered freely at the glomerulus and 50% is reabsorbed at the proximal tubule.

As the tubular fluid passes down the descending limb, the urea concentration is increased by:

- The passage of water out of the descending limb.
- The addition of urea that moves freely from the medullary interstitium at the tip of the loop (an area of high urea concentration caused by collecting tubules) (see later).

C) The Distal Tubule:

1- The distal tubules receive hypotonic fluid from the loop of Henle. It is relatively **impermeable to H_2O and Na^+;** therefore, it maintains the osmolality gradients generated by the loop of Henle.

2- **Na^+ ($H2O$, K^+, and HCO_3^-) reabsorption** occurs (about 5%) by:

- Na^+-Cl^- carrier on the luminal border (symporter transport). It is the site of action of thiazide diuretics.
- Na^+-K^+-ATPase dependant pump that is located on the capillary side.
- Na^+ reabsorption that is stimulated by **aldosterone** at the late part of that distal tubule.

3- **Ca^{++} reabsorption** that is stimulated by parathyroid hormone.

4- **Secretion of H^+, K^+, and Ca^{++}** that also occurs in the distal tubules.

D) The Collecting Tubule:

It reabsorbs about **4%** of glomerular filtrate (i.e., it reabsorbs **NaCl, H_2O, K^+, and HCO_3^-**) where 5% of glomerular filtrate enters the collecting ducts and about 1% leaves it as urine. The collecting ducts also the secrete **K^+ and H^+.** It is also responsible for **ammonia production.**

a- Cortical Collecting Tubule:

It is formed of 2 types of cells:

1- Principal Cells (P Cells):

They reabsorb Na^+ via electrogenic pump. Either Cl^- must be also reabsorbed or K^+ must be secreted to maintain electro-neutrality.

Na^+ reabsorption is Na-K ATPase dependant and is stimulated by aldosterone.

2- Intercalated Cells (I Cells):

They are responsible for acid-base regulation as:

- Aldosterone stimulates H^+ and K^+ secreting ATPase on its luminal border.
- There is K^+-H^{-+} ATPase pump on the luminal border which reabsorbs K^+ and secretes H^+.
- They can secrete HCO_3^- ions in response to large alkali loads.

b- Medullary Collecting Tubule:

Anti-diuretic hormone (ADH) (also called **arginine vasopressin)** stimulates V_2 receptors which stimulate adenyl cyclase enzyme resulting in water reabsorption.

N.B.: V_1 receptors increase vascular resistance by promoting phosphatidyl inositol turnover.

Dehydration increases ADH which increases H_2O permeability resulting in decreasing urine volume and increasing urine concentration up to 1400 mOsmol/L. The reverse occurs with over-hydration as it decreases ADH which decreases H_2O permeability, so the urine volume increases and its concentration decreases down to 100-200 mOsmol/L.

c- Role of Collecting Tubule in Medullary Hyper-tonicity:

The cortical collecting tubules are impermeable to urea, but permeable to H_2O, which increases urea concentration within the tubules.

The medullary collecting tubules are permeable to both H_2O and urea under the effect of ADH, so when ADH is secreted, both H_2O and urea diffuse to the medullary interstitium leading to an increase in its tonicity.

Renin Angiotensin System

Synthesis, action and catabolism of renin angiotensin system are discussed in (figure 16-8). Some external production of renin and angiotensin II occur in vascular endothelium, adrenal glands, and brain.

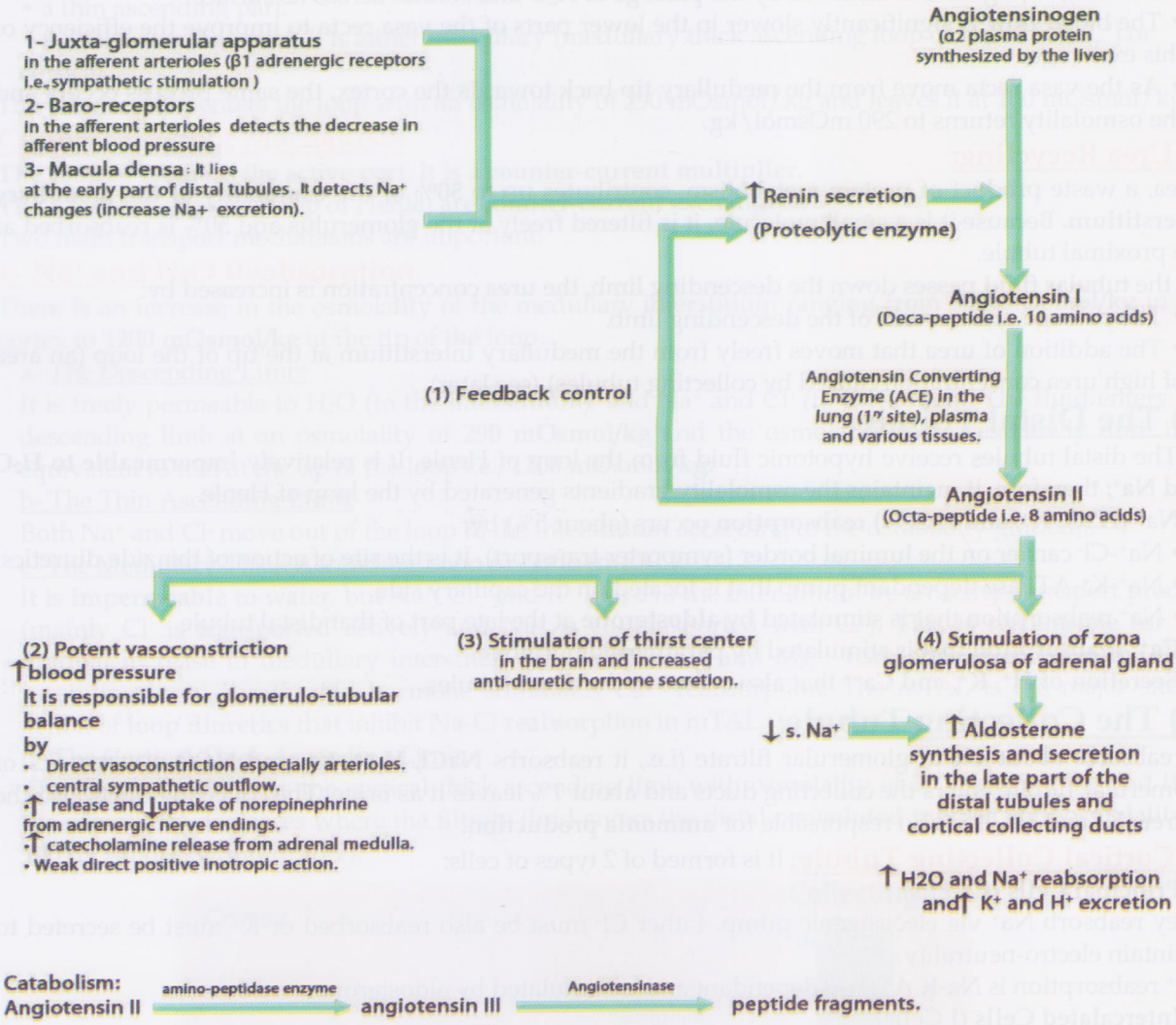


Figure 16-8: Angiotensin-Aldosterone System

Renal Regulation of Acid-Base Balance

Up to 80-90% of HCO_3^- is reabsorbed in the proximal tubules and the remainder 10-20% in the distal tubules. The reverse occurs with H^+ ions as they are secreted in distal tubules while some are secreted in proximal tubules (figure 16-9).

H^+ ions come from dissociation of intracellular carbonic acid.

1/3 of H^+ is excreted as sodium dihydro phosphate (NaH_2PO_2) (i.e. titrable acid).

2/3 of H^+ is excreted as quaternary ammonium (NH_4^+).

Total H^+ secretion = NH_4^+ excretion + Titrable acid excretion – HCO_3^- excretion.

Osmolar Regulation

Final urine volume depends on: • the extracellular fluid volume and its regulation via Na^+ excretion.
• regulation of plasma osmolarity.

Osmolar regulation system is discussed in the chapter of "Fluid & Electrolyte Disturbances".

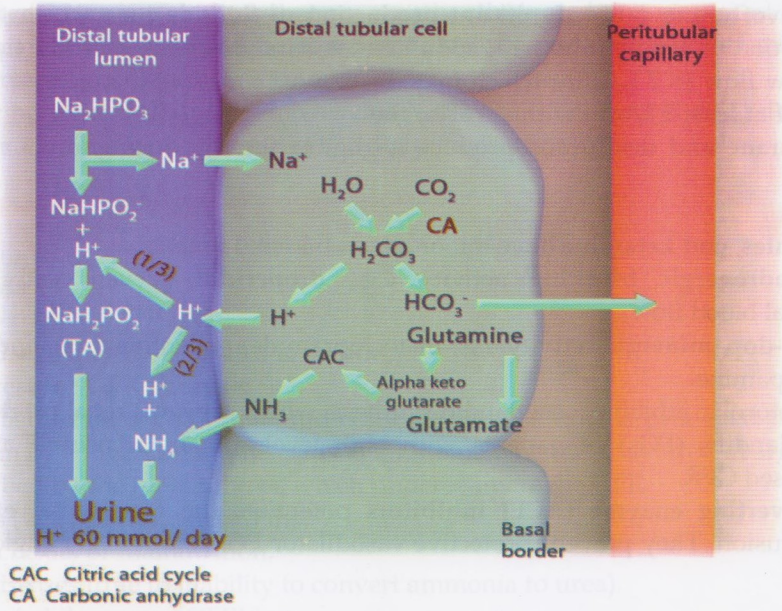


Figure 16-9: Hydrogen excretion in the distal tubules

Effects of Anesthesia on Renal Function

a- Indirect Effects:

1- Cardiovascular Effects:

• Most general anesthetics produce cardiac depression and vasodilation and regional anesthetics block the sympathetic system causing vasodilation. Both **decrease blood pressure below the limits of autoregulation** resulting in decreased renal blood flow. I.v. fluids can partially reverse these effects.

2- Neural Effects:

Factors stimulate **sympathetic activity** causing **vasoconstriction of renal vessels** resulting in decreased renal blood flow e.g., • Anesthesia induced circulatory depression.

- Intense surgical stimulation.
- Tissue trauma.
- Light anesthesia.
- Hypoxia.
- Acidosis.

3- Endocrine Effects:

The above factors also can induce the **stress response** resulting in an increase in **catecholamines, anti-diuretic hormone, and renin angiotensin**. These hormones cause vasoconstriction of renal vessels resulting in decreasing renal blood flow.

Generally, anesthesia decreases renal blood flow resulting in **a decrease in glomerular filtration rate (GFR)** which in turn **decreases the urine output**.

N.B.: Surgical Effects on Renal Function

Renal function can be affected by one of these surgical maneuvers:

- The pneumoperitonium produced during laparoscopy.
- Cardiopulmonary bypass.
- Cross-clamping of the aorta.
- Dissection near the renal arteries.

All decrease renal blood flow and glomerular filtration rate. They are discussed in their corresponding chapters.

b- Direct Effects:

1- Volatile Agents:

• **Methoxyflurane is nephrotoxic.** Its nephrotoxicity is dose related (i.e., > 2.5-3 MAC hours exposure i.e., exposure to MAC for 2.5-3 hours). It increases the release of fluoride ions from its metabolism (> 50 μmol/L) resulting in a defect in the urine concentrating ability (syndrome of polyuric renal failure or nephrogenic diabetes insipidus).

• **Enflurane and sevoflurane** cause significant production of fluoride ions which theoretically causes renal effects. Interaction of sevoflurane with soda lime or baralyme causes production of compound A especially at very low flow (< 2 L/min) which may affect renal function; therefore, it is recommended to use **fresh gas flow of at least 2 L/min with sevoflurane**.

• **Halothane, isoflurane and desflurane** produce negligible fluoride ions and so, no renal effects are produced.

2- Intravenous Agents:

• **Opioids, barbiturates, and ketamine** have minor effects on renal function.

• Drugs with **α-adrenergic blocking** activity e.g., **droperidol** prevent catecholamine induced redistribution of renal blood flow.

• Drugs with **α-anti-dopaminergic activity** e.g., metoclopramide, phenothiazines, and droperidol impair renal response to dopamine.

• **Analgesics** e.g., ketorolac inhibit prostaglandin synthesis which prevents renal production of protective vasodilator prostaglandins (PGs) in patients with high levels of angiotensin II and norepinephrine resulting in a decreased GFR.

• **Angiotensin converting enzyme (ACE) inhibitors** potentiate the detrimental effects of anesthetic agents on renal perfusion. They prevent protective vasodilator PGs, induced by angiotensin II, resulting in a decreased GFR.

3- Other Agents:

• **Antibiotics (e.g., aminoglycosides and amphotericin B).**

• **Immunosuppressive agents (e.g., cyclosporine and tacrolimus):** Pretreatment with Ca^{++} channel agents (diltiazem) may produce renal protection.

• **Radiocontrast dyes:** Pretreatment with acetylcysteine has a renal protective effect due to its free radical scavenging or sulfhydryl donor (reducing) properties.

Effect of Renal Disease on Pharmacokinetics of Drugs

In renal failure or impairment:

• **Highly protein-bound drugs** (such as acidic drugs which bind mainly to albumin) have an **increased unbound, active, free fraction** in renal failure. A decrease in serum albumin concentration, an increase in serum urea concentration, and the competition between endogenous substrates and drug metabolites for plasma protein binding sites lead to a decrease in the plasma protein binding of these drugs. **The doses of these drugs should be decreased 20-50%** e.g., thiopental, methohexitol, and diazepam.

• **Drugs depending on renal (and hepatic) elimination;** when administered by bolus or short-term infusion, their elimination depends on redistribution in the extracellular fluid compartment and not elimination. Therefore,

a- For the loading doses:

▫ In patients with normal extracellular fluid compartment and with renal dysfunction (or hepatic dysfunction), **use the standard loading doses** (i.e., it is usually **not necessary to decrease the initial loading dose.**

▫ In patients with clinically contracted extracellular fluid compartment, the loading dose should be reduced.

▫ In patients with clinically expanded extracellular fluid compartment, the loading dose should be increased.

b- For the maintenance doses: The **subsequent maintenance doses** may cause drug accumulation and should be **reduced** appropriately and titrated carefully to effect as follows:

▫ Drugs with wide therapeutic ranges or long plasma half-lives, the interval between doses should be increased.

▫ Drugs with narrow therapeutic ranges or short plasma half-lives, the prescribed doses should be decreased.

A combination of both methods is frequently used according to the glomerular filtration rate.

These drugs are either totally eliminated by the kidneys such as digoxin, penicillins, cephalosporins, aminoglycosides, vancomycin, cyclosporine A, and tacrolimus or are partially eliminated by the kidneys such as anticholinergics, cholinergics, pancuronium, pipecuronium, vecuronium, aminocaproic acid, and tranexamic acids.

• **Several drugs have active metabolites that are renally eliminated** that may exert a prolonged effect in renal failure. The parent drugs should be **avoided or strictly curtailed** such as midazolam, morphine, meperidine, procainamide, and sodium nitroprusside.
• **Hemodialysis or peritoneal dialysis** removes drugs of low molecular weight and low protein-binding. These drugs are usually re-given at the end of the dialysis schedule.

Evaluation of Renal Function

A) Blood Tests

1- Blood Urea Nitrogen (BUN):

Normal values = **10 – 20 mg/dL = 1.6 – 3.3 mmol/L.**
It is **not a reliable test for GFR because:**

- Protein catabolism should be normal and constant because urea is produced from the liver during protein catabolism by converting amino acids to ammonia which is converted in arginine cycle to urea.
- Urea is reabsorbed by the renal tubules which underestimate the GFR.
- BUN decreases (with GFR is normal) in:
  - starvation, cachexia, or malnutrition.
  - severe liver diseases (due to inability to convert ammonia to urea).
- BUN increases (while normal GFR) in:
  - increased protein catabolism e.g., sepsis, trauma, or steroid-induced catabolic activity.
  - increased protein intake such as blood degradation in gastrointestinal tract or in hematoma or high protein diet.
  - edematous disorders such as congestive heart failure, cirrhosis, and nephrotic syndrome.
  - dehydration (prerenal causes).
  - obstructive uropathy.

Normally, 35-50% of filtered urea is reabsorbed by renal tubules. Under conditions of decreased renal blood flow (such as the above conditions), tubular reabsorption of urea can increase to 90% or more due to the slow rate of fluid flow via the renal tubules resulting in more time for anti-diuretic hormone action. This increases urea (but not creatinine) reabsorption. Since creatinine is not reabsorbed, serum urea increases more rapidly than serum creatinine under these conditions resulting in increased BUN: creatinine ratio > 20.
BUN increases usually > 50 mg/dL with decreased GFR.

2) Serum Urea:

Normal value = **20 – 40 mg/dL** = 2.7 – 7.0 mmol/L.

3) Serum Creatinine:

Normal value = **0.6 – 1.3 mg/dL = 0.045 – 0.12 mmol/L.**
Serum creatinine is derived non-enzymatically from creatine which is a product of muscle metabolism. Because the body muscle mass is usually fairly constant, serum creatinine measurements are generally reliable indices of GFR, but serum creatinine is an **unreliable marker of GFR in the following conditions**:

- **In a cachectic patient** with depleted muscle mass, creatinine generation may be so low that serum creatinine remains < 0.9 mg/dL in the face of a GFR < 25 mL/min.
- In rapidly changed renal function, for example, suprarenal aortic cross-clamping creates a zero GFR state, but serum creatinine will still be at baseline, and it may take days before a new equilibrium is established where serum creatinine represents zero GFR. When GFR starts to recover, serum creatinine will continue to rise until creatinine excretion equals creatinine. Also in acute renal failure, GFR decreases from 100 mL/min to 10 mL/min while serum creatinine values do not increase correspondingly for approximately 7 days i.e., **serum creatinine values are slow to reflect acute changes**
- Serum creatinine increases (without a decrease in GFR) in:
  - Large meat meals.
  - Cimetidine therapy as it inhibits creatinine secretion by renal tubules.
  - Increased acetoacetate (as during ketoacidosis) that interferes with laboratory methods for measuring creatinine.
- **GFR decreases with age** (5% per decade after the age of 20 years), but because muscle mass also decreases, serum creatinine remains relatively normal.

Serum creatinine increases with decreased GFR. From the figure 16-10, each doubling of serum creatinine represents a 50% reduction in GFR.

4) Serum Osmolality:

Normal value = **280 – 300 mOsmol/L.**

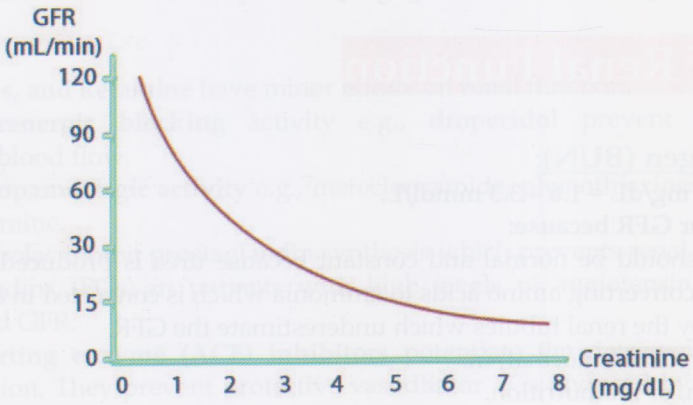


Figure 16-10: Serum creatinine and GFR

B) Clearance Tests

1) Inulin Clearance:

It is the gold standard clearance test because it equals the **GFR.** Its normal value = **100 – 150 mL/min.**

2) Para-Amino-Hippuric Acid Clearance:

It equals **renal plasma flow.** Its normal value = **560 – 830 (600) mL/min.**

3) Creatinine Clearance:

It is considered the best clinical measure of renal function and the most reliable test. It nearly equals **GFR.**
Its normal value = **100 – 120 mL/min.**
It can be calculated by two different methods:

- Creatinine clearance = $\frac{[\text{Creatinine}]\text{Urine (mg/dL)} \times \text{Urinary flow (mL/min)}}{[\text{Creatinine}]\text{Plasma (mg/dL)}}$ mL/min

It needs accurate urine collection over a specified period of time. 24 hour urine collection has been needed to eliminate error induced by residual urine in the bladder, but in good hydrated spontaneously voiding out patients, or catheterized in-patients, carefully timed 1-2 hour urine collection can be used to give accurate creatinine clearance.

- **Cockcroft and Gault formula** as follows:

$$\text{Estimated creatinine clearance (mL/min)} = \frac{[140 \quad \text{age (years)}] \times \text{ideal or lean body weight (kg)}}{72 \times \text{serum creatinine (mg/dL)}}$$

In women, the result should be multiplied by 0.85 due to a smaller muscle mass.
In obese patients with body mass index ≥ 30, ideal or lean rather than actual body weight should be used.
This equation is a crude estimation of creatinine clearance.

Creatinine clearance is a very reliable test in assessing kidney function. Patients are divided into:

	Creatinine Clearance (mL/min)	Clinical picture
Normal kidney function	100 – 120	No clinical picture
Decreased renal reserve	60 – 100	No clinical picture
Mild renal impairment	40 – 60	No clinical picture
Moderate renal impairment (renal insufficiency)	25-40	Nocturia
Renal failure (renal failure)	< 25	Clinical picture of Uremia
End stage renal disease (chronic renal failure)	10	Clinical picture of Uremia

4) Urea Clearance:

It can be used as creatinine clearance, but it needs 24 hour urine collection because 2 hour urine collection is not useful with urea clearance.

C) BUN: Creatinine Ratio

Normal BUN: creatinine ratio = 10:1.

Decreased renal tubular flow rates (see above for causes) increase urea absorption, but do not affect creatinine; therefore, the ratio is increased up to > 20: 1.

D) Urine Analysis

The urine sample is examined for the following:

Urine pH: If it is > 7.0 (with blood acidosis), this indicates renal tubular acidosis.

Specific Gravity:

Specific gravity is the density of the urine in relation to the water. Its normal range = **1.003 – 1.040**.

If it is > 1.018 after overnight fasting, this indicates adequate renal concentration ability.

If it is decreased and associated with plasma hyper-osmolality, this indicates diabetes insipidus.

Urine Osmolality: Normal range = 300-1200 mOsmol/kg.

Urine Creatinine: Normal range = 0.85 – 17.1 mmol/L.

Urine Sodium Excretion: Normal range = < 40 mmol/L (mEq/L).

- Decreased urine sodium excretion < 15-20 mmol/L occurs when normally functioning renal tubules conserve sodium in the presence of hypovolemia and the urine osmolarity is likely to exceed 500 mOsmol/L due to increased Na^+ reabsorption.
- Increased urine sodium excretion > 40 mmol/L usually with urine osmolarity < 350 mOsmol/L occurs with: hypoxemia affecting damage of renal tubules (i.e., chronic renal failure) or drug-induced diuresis,

where there is decreased Na^+ reabsorption due to the renal disease itself.

The Fractional Excretion of Sodium (FE_{Na}) %

$$FE_{Na} = \frac{\text{Na Clearance}}{\text{Creatinine Clearance}}$$

$$= \frac{\text{Urine Na (mEq/L)}}{\text{Urine Creatinine (mg/dL)}} \times \frac{\text{serum Creatinine (mg/dL)}}{\text{serum Na (mEq/L)}} \times 100$$

The normal value of FE_{Na} is < 1% i.e., less than 1% of the filtered Na is excreted in the urine.

FE_{Na} can differentiate between prerenal azotemia and acute tubular necrosis as follows:

- Prerenal azotemia is associated with FE_{Na} < 1% and urine output < 500 mL/day.
- Acute tubular necrosis is associated with FE_{Na} > 1% and urine output < 500 mL/day.

In acute tubular necrosis due to myoglobinuria FE_{Na} can be < 1%

The value of this test is lost if diuretics are given prior to collection of the urine sample such as in patients with congestive heart failure receiving loop diuretics.

$$\textbf{Renal failure index} = \frac{\text{Urine Sodium (mmol/L)}}{\text{Urine creatinine (mg/dL)/ Serum creatinine (mg/dL)}}$$

In prerenal azotemia it is < 1% while in acute tubular necrosis it is > 1%.

The Fractional Excretion of Urea (FE_{Urea}) %

$$FE_{Urea} = \frac{\text{Urea Clearance}}{\text{Creatinine Clearance}}$$

$$= \frac{\text{Urine Urea (mg/dL)}}{\text{Urine Creatinine (mg/dL)}} \times \frac{\text{Serum Creatinine (mg/dL)}}{\text{Serum Urea (mg/dL)}} \times 100$$

Normal values in well-hydrated individuals are between **50% and 65%.**

Values below 35% are most compatible with **renal hypoperfusion** and are not affected by loop diuretics such as furosemide. So, it is useful in patients taking diuretics as in congestive heart failure.

A markedly diminished FE_{Urea} cannot distinguish between a rapidly reversible prerenal azotemia and more definitive ischemic damage, such as that occurs in acute tubular necrosis. Osmotic diuresis resulting

from administration of mannitol or acetazolamide or from diabetic ketoacidosis increases the FE_{Urea} despite the existence of volume depletion.

Glucosuria: Normally, it is absent. It occurs in: • Decreased renal threshold (N = 180 mg/dL).
• Hyperglycemia.

Proteinuria:

Normal proteinuria (albumin) is usually < 150 mg/day.

Causes of proteinuria > 150 mg/day:

a- **Transient proteinuria:** It resolves with treatment of the underlying illness such as:
• Fever. • Exercise. • Congestive heart failure • Seizure activity. • Pancreatitis.

b- **Orthostatic proteinuria:** It occurs in up to 5% of adolescents while they are in the upright position and resolves when the recumbent position is assumed. Orthostatic proteinuria resolves spontaneously and is not associated with any deterioration in renal function.

c- **Persistent proteinuria:** It indicates significant renal disease.
Microalbuminuria is the earliest sign of diabetic nephropathy.
Proteinuria > 1 g/day usually occurs in many forms of acute renal failure.
Proteinuria > 3.5 g/day usually occurs in nephrotic syndrome (i.e., due to a glomerular disease).

Severe proteinuria may result in hypoalbuminemia, with associated decreases in plasma oncotic pressure and decreased protein binding of drugs.

Bilirubinuria:

It is increased bilirubin in the urine which indicates biliary obstruction.

Microscopic Analysis of the Urinary Sediment:

• **Free red blood cells** in the urine indicate bleeding anywhere between the glomerulus and urethra e.g., tumors, stone, infection (glomerulonephritis), trauma (by a catheter), sickle cell disease and coagulopathy.
• **Red blood cell casts** are pathognomic of acute glomerulo-nephritis or vasculitis.
• **White blood cells and white blood cell casts or bacteria** indicate infection (pyelonephritis or interstitial nephritis).
• **Tubular or oval epithelial casts and granular casts** indicate a disease of the nephrons (acute tubular necrosis or interstitial nephritis).
• **Muddy-brown casts** indicate acute tubular necrosis.
• **Pigmented casts** indicate myoglobinuria.
• **Hyaline casts** indicate prerenal ischemia.
• **Crystals** indicate abnormal metabolism of oxalic acid, uric acid, and cysteine.

Urine Culture and Gram Staining should be performed on any urine containing white blood cells. **Sterile pyuria** is often a sign of drug-induced interstitial nephritis, but renal tuberculosis also should be considered.

Differentiation between Causes of Oliguria:

U = Urine P = Plasma	Normal Value	Prerenal Causes e.g., dehydration	Renal Failure (Acute tubular necrosis)
a- Plasma: - Urea : creatinine ratio	10 : 1	> 20 : 1	< 10 : 1
b- Urine: - Specific gravity - Urine Na^+ mmol/L - Osmolality mOsmol/kg - Urine sediment	1.000 – 1.040 40 - 140 300 - 1200 Normal	> 1.022 < 20 > 400 Normal or hyaline cast	1.010 – 1.012 > 40 < 350 Tubular (oval), granular, or muddy-brown casts
c- U/P ratio - U/P Urea ratio - U/P Creatinine ratio - U/P Osmolality ratio - FE_{Na} - Renal failure index - FE_{Urea}	> 20 : 1 > 2 : 1 < 1% 50 - 65%	> 20 : 1 > 40 : 1 > 2.1: 1 < 1% < 1% < 35%	< 10 : 1 < 10 : 1 < 1.2 : 1 > 1% > 1%

N.B.: Both FE_{Na} and renal failure index are **the most sensitive tests.** In **prerenal failure**, Na^+ is reabsorbed avidly from glomerular filtrate to restore intravascular volume, but in **renal failure**, is does not occur due to epithelial injury. Creatinine is less efficiently reabsorbed less efficiently in both cases.

Anesthesia for Patient with Renal Impairment or Failure

Acute Renal Failure

Definition:

A rapid deterioration in renal function over a period of **hours to days** resulting in failure of the kidney to excrete waste products with retention of nitrogenous waste products (azotemia) which include urea, guanidine compounds (as creatine, creatinine)...etc with failure to maintain fluid and electrolyte homeostasis. If it is not treated, irreversible acute renal failure occurs.

Other Definitions:

- An increase in serum creatinine concentrations of more than 0.5 mg/dL compared with a baseline value,

or • a 50% decrease in the calculated creatinine clearance.

Incidence:

It is 5-7% of all hospitalized patients.

Causes: (Causes of Perioperative Oliguria)

a) Pre-renal Causes (Ischemia): i.e., acute decrease in renal perfusion.

- Hypovolemia or other causes of hypovolemic shock such as hemorrhagic shock, burn...etc.
- Hypotension i.e., decreased mean blood pressure below the limits of renal autoregulation (< 80 mm Hg).
- Drugs that impair autoregulation such as non-steroidal anti-inflammatory drugs (ketorolac), angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers.
- Low cardiac output e.g., congestive heart failure, cardiomyopathy, mechanical ventilation, aortic stenosis, dissecting aortic aneurysm.
- Renal artery stenosis.

b) Renal Causes:

1- Acute tubular necrosis is the most common cause (50%).

It is characterized by oxidative injury to the renal tubular epithelial cells with sloughing of cells into the lumen of the renal tubules. The sloughed cells create an obstruction that increases the pressure in the proximal tubule decreasing GFR. Acute tubular necrosis occurs due to the following causes:

- All causes of prerenal ischemia if severe and prolonged.
- Nephrotoxins:
  - Endotoxins:
    - Hemoglobin from mismatched blood transfusion.
    - Myoglobinuria.
    - Porphyria.
    - Gram negative septicemia (sepsis).
    - Bilirubin in obstructive jaundice.
  - Exotoxins:
    - Antibiotics as sulphonamide amphotericin B, cisplastin, or garamycin.
    - Radiographic contrast dye: Renal failure usually occurs 72 hours after the procedure. Most cases resolve within 2 weeks and few require hemodialysis. Acute tubular necrosis occurs due to hyperosmolar or oxidative injury to the renal tubular epithelial cells. It is more common in patients with diabetes mellitus, hypertension, pre-existing renal disease, or congestive heart failure.
    - Heavy metals: mercury or phenol.
    - Solvents as carbon tetrachloride ethylene glycol.

2- Acute glomerulo-nephritis.

3- Acute interstitial nephritis: It is an inflammatory condition that involves the renal Interstitium usually due to sepsis or drugs such as:

- Antibiotics (aminoglycosides, amphotericin B, cephalosporins, penicillins, sulfonamides, or vancomycin).
- Neurological drugs (carbamazepine, phenobarbital, and phenytoin).
- Non-steroidal anti-inflammatory drugs (aspirin, ibuprofen, ketorolac, or naproxen).
- Diuretics (acetazolamide, furosemide, or thiazides).
- Others (acetaminophen, angiotensin-converting enzyme inhibitors, iodinated dyes, or ranitidine).

c) Post-renal Causes:

Urinary tract obstruction either bilateral or unilateral with single functioning kidney. It is either:

- Upper urinary tract obstruction e.g.,
  - ureteric obstruction such as a retroperitoneal mass, stone, or stricture.
  - ligation of both ureters during surgery.
- Lower urinary tract obstruction e.g.,
  - bladder outlet obstruction such as prostatic hypertrophy, cancer of prostate, cervix, or bladder.
  - compression of bladder by retractors during surgery.

Clinical Picture:

1- Urine output: can be one of the following states:

- **Anuric renal failure:** The urine output is **< 100 mL/day up to complete anuria** (unusual and may occur in post-renal causes).
- **Oliguric renal failure:** The urine output is **< 400 mL/day (< 0.5 mL/kg/hour)**. It is the most common. It lasts usually for **2 weeks** and then is followed by the diuretic phase with progressive increase in urine output then renal functions improve over several weeks up to 1 year.

- **Non-oliguric renal failure:** The urine output is **> 400 mL/day**. It is the least severe form.

2- Systemic clinical picture: includes neurological problems (confusion, somnolence…etc), cardiovascular problems (hypertension, hypotension, congestive heart failure, pulmonary edema, and arrhythmias), gastrointestinal problems (anorexia, nausea, vomiting, ileus …etc.) and infections (respiratory, urinary tract…etc.). They are similar to chronic renal failure.

Investigations:

1- Investigations to detect the cause such as renal ultrasonography or x-ray…etc.
2- Investigations for the acute renal failure such as serum creatinine …etc.
3- Investigations for differentiation between pre - and renal causes (see before).

Management of Acute Renal Failure

1- Treatment of possible causes e.g., hypovolemia, hypotension…etc.

2- Renal Prophylactic Therapy (Renal Protection):

- **Appropriate hydration** and optimal preservation of the intravascular fluid volume is the only proven therapy in prevention and early treatment of acute renal failure. Fluid therapy should be titrated to maintain central venous pressure at 10-15 cm H_2O.

The problems of over-hydration such as pulmonary edema and congestion are easier to be treated than problems of under-hydration such as acute renal failure.

- **Maintenance of adequate systemic blood pressure** (**minimum mean blood pressure 65 mmHg** in normotensive and 85 mmHg in hypertensive patients) and **cardiac output** to prevent peripheral vasoconstriction.
- **Avoidance of potential nephrotoxins** (see the above drugs).

N.B: Renal preventive measures before radiographic contrast dye injection include:

- I.v. hydration (if permitted) that should started by injection of the dye to maintain urine output at 150 mL/hour for at least 6 hours after the procedure.
- N-acetylcysteine: It is a reactive oxygen metabolite scavenger which is given as follows:
  600 mg oral twice daily from 24 hours before, to 24 hours after the procedure, or 600 mg i.v. just before the procedure, and
  600 mg oral twice daily for 48 hours after the procedure.

- Maintenance of Urine Output (after adequate hydration):

Maintenance of urine output has been formerly recommended, but it has been demonstrated by randomized controlled trial to be ineffective. Diuretics are used as follows:

1- **Mannitol infusion with good hydration** is very beneficial in some cases especially jaundiced patients or with rhabdomyolysis. Mannitol **improves** outcome and decreases morbidity and mortality.

2- **Furosemide injections or infusions** change the urine output from oliguric to normal amounts. It is useful **in some cases** as crush injuries. In some cases of oliguric acute renal failure, where adequate resuscitation has failed to achieve diuresis, furosemide i.v. does appear to **"Kick-start"** a urine output which is then maintained.

3- **Dopamine does not improve** morbidity or mortality in acute renal failure, but actually has deleterious effects on: ▫ hemodynamics (due to reduction of splanchnic blood flow),

- immune function (due to inhibition of T-cell lymphocyte function), and
- endocrine system (due to inhibition of thyroid stimulating hormone release from the pituitary gland).

3- Supportive Management:

- Correction of fluid, electrolyte, and acid-base derangements.
- **Dialysis or hemo-ultrafiltration** is still the most important therapy **in severe** acute renal failure.

Anesthetic Management in Patients with Acute Renal Failure

- The same principles are used during **prophylactic and supportive measures** of acute renal failure as discussed above.
- **Only life-saving surgery** should be undertaken in such a patient.
- **Invasive monitors** are necessary such as arterial blood gases, electrolytes, invasive blood pressure...etc.

RIFLE

- RIFLE is a newly developed international consensus classification for acute kidney injury. Acute kidney injury is generally defined as "an abrupt and sustained decrease in kidney function".
- RIFLE defines three grades of increasing severity of acute kidney injury – **R**isk (class R), **I**njury (class I) and **F**ailure (class F) – and two outcome classes (**L**oss and **E**nd-stage kidney disease).
- Acute kidney injury occurred in 67% of intensive care unit admissions, with maximum RIFLE class R, class I and class F in 12%, 27% and 28%, respectively.
- Patients with maximum RIFLE class R, class I and class F had hospital mortality rates of 8.8%, 11.4% and 26.3%, respectively, compared with 5.5% for patients without acute kidney injury.

Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) classification:

Class	Glomerular filtration rate criteria	Urine output criteria
Risk	Serum creatinine × 1.5	< 0.5 ml/kg/hour × 6 hours
Injury	Serum creatinine × 2	< 0.5 ml/kg/hour × 12 hours
Failure	Serum creatinine × 3, or serum creatinine ≥ 4 mg/dl with an acute rise > 0.5 mg/dL	< 0.3 ml/kg/hour × 24 hours, or anuria × 12 hours
Loss	Persistent acute renal failure = complete loss of kidney function > 4 weeks	
End-stage Kidney Disease	End-stage kidney disease > 3 months	

For conversion of creatinine expressed in conventional units to SI units, multiply by 88.4. RIFLE class is determined based on the worst of either glomerular filtration criteria or urine output criteria. Glomerular filtration criteria are calculated as an increase of serum creatinine above the baseline serum creatinine level. Acute kidney injury should be both abrupt (within 1–7 days) and sustained (more than 24 hours). When the baseline serum creatinine is not known and patients are without a history of chronic kidney insufficiency, it is recommend to calculate a baseline serum creatinine using the Modification of Diet in Renal Disease equation for assessment of kidney function, assuming a glomerular filtration rate of 75 ml/min/1.73 m^2. When the baseline serum creatinine is elevated, an abrupt rise of at least 0.5 mg/dl to more than 4 mg/dl is all that is required to achieve class Failure.

Renal Insufficiency and Chronic Renal Failure (Uremia)

Definition:

It is a progressive and irreversible decrease in renal functions over the course of at least **3-6 months.**
The term "uremia" is derived from increased serum urea in patients with renal failure.

Causes:

1- Diabetic nephropathy is the most common cause (53%).
2- Hypertensive nephron-sclerosis is the second common cause.
3- Chronic glomerulo-nephritis.
4- Polycystic kidney disease (with normal urine output, but without concentrating ability).

5- Other causes as pyelonephritis, lupus erythematosis, vasculitis, amyloidosis, analgesic nephropathy, sarcoidosis, obstructive uropathy, renal vascular diseases, human immuno-deficiency virus and congenital anomalies.

Clinical Picture:

The clinical picture starts to occur when GFR (and creatinine clearance) becomes **25-40 mL/min (i.e., renal impairment)** and becomes **more obvious** when GFR becomes **< 25 mL/min (i.e., chronic renal failure)**.

The clinical picture **may be undetectable** until the later stages of the disease and even then often continue to be **nonspecific and vague** appearing **insidiously** as fatigue, general malaise, pruritis, anemia, anorexia, nausea, and vomiting (this is called **uremic syndrome**). The severity of clinical picture and the response to therapy is related to blood urea nitrogen (BUN) concentration (and not serum creatinine).

1) Central Nervous System:

- Peripheral neuropathy mainly sensory in lower limbs such as paresthesia.
- Autonomic neuropathy which may manifest as orthostatic hypotension (and impaired circulatory response to anesthesia), delayed gastric emptying, or silent myocardial ischemia.
- Muscle twitching.
- Encephalopathy which manifests as astrexis, myoclonus, lethargy, confusion, seizures, and coma.

2) Cardiovascular System:

- Fluid overload and hypoalbuminemia which result in congestive heart failure. This causes peripheral and pulmonary edema, but sometimes unpredictable intravascular fluid status is present.
- Hypertension due to ▫ decreased juxta-glomerular apparatus perfusion which increases renin level, and ▫ fluid overload.
- Arrhythmias.
- Conduction block due to Ca^{++} deposits in the conductive system.
- Uremic pericarditis, pericardial effusion or tamponade.
- Accelerated atherosclerosis due to hyperlipidemia.
- Hyperdynamic circulation (i.e., high cardiac output heart failure) due to
  - ▫ anemia,
  - ▫ arterio-venous shunt of the dialysis.

3) Pulmonary System:

- Acidosis resulting in hyperventilation.
- Alveolar and interstitial pulmonary edema resulting in hypoxia.
- Pleural effusion.

4) Gastrointestinal Tract (Uremic Enteropathy):

- Anorexia, nausea, vomiting, hiccup, and under-nutrition.
- Delayed gastric emptying due to autonomic neuropathy.
- Hyperacidity which may lead to ulceration (peptic ulcer) and gastrointestinal bleeding.
- Adynamic ileus.
- Esophagitis, gastritis, enteritis, colitis, or proctitis.

5) Endocrine System:

- Glucose intolerance and hyperglycemia due to peripheral resistance to insulin.
- Hyper-triglyceridemia (due to decreased lipoprotein lipase activity) resulting in atherosclerosis.
- Secondary hyperparathyroidism which causes hyperphosphatemia and vitamin D depletion. These cause bone resorption and decreased Ca^{++} absorption which causes bone disease.

6) Skeletal System:

- Renal osteo-dystrophy: As the GFR decreases, there is a parallel decrease in phosphate clearance and an increase in the serum phosphate concentrations that result in reciprocal decreases in serum calcium concentrations. Hypocalcemia stimulates parathyroid hormone secretion, which leads to bone resorption and calcium release. As a result of decreased renal production of vitamin D by the diseased kidneys, intestinal absorption of calcium is impaired, which also leads to hypocalcemia, stimulation of parathyroid hormone release, and bone resorption.
- Peri-articular calcifications due to Ca^{++} deposition secondary to hyperphosphatemia.

7) Metabolic System:

- Metabolic acidosis:

- Early, a hyperchloremic non-anion gap metabolic acidosis can occur due to bicarbonate wasting (renal tubular acidosis).
- Later, a high anion gap metabolic acidosis occurs once chronic renal failure is established due to retained non-volatile acids, sulfate and phosphates.

• Hyperkalemia (hypokalemia may occur if the patient is on diuresis).
• Hypernatremia (hyponatremia may occur due to pyelonephritis, analgesic nephropathy, vomiting, diarrhea or diuretics).
• Hypermagnesemia especially if the patient is taking Mg^{++} containing antacids.
• Hyperuricemia.
• Hyperphosphatemia.
• Hypocalcemia due to:
  - Ca^{++} deposition peri-articularly by hyperphosphatemia.
  - decreased Ca^{++} absorption from the gut due to decreased renal synthesis of 1,25 dihydroxy cholecalciferol (vitamin D).
• Hypoalbuminemia.

8) **Hematological System:**
• Normochromic anemia (usually 5-7 g%) due to:
  - Decreased erythropoietin production resulting in decreased red blood cell production.
  - Decreased red blood cell survival.
  - Bone marrow suppression due to repeated infections, uremia, and aluminum toxicity.
  - Gastrointestinal bleeding.
  - Hemodilution.
  - Excess parathyroid hormone replaces bone marrow with fibrous tissues.
• White blood cell dysfunction: It increases susceptibility to infections.
• Platelet dysfunction due to decreased endothelial release of factor VIII (and von Willebrand factor) resulting in increased bleeding time with increased bleeding tendency such as gastrointestinal bleeding, epistaxis, hemorrhagic pericarditis, and subdural hematoma.

9) **Skin:**
• Hyper-pigmentation.
• Ecchymosis.
• Pruritis.

10) **Complications of Dialysis (in Patients with Chronic Renal Failure)**
Such as dementia, dialysis disequilibrium syndrome, volume depletion, hypotension, arrhythmias…etc. More details are discussed later.

Q: Discuss intensive care management of renal failure?
A: The management of acute and chronic renal failure (causes, clinical pictures, investigations and treatment) should be discussed.

Preoperative Management

Preoperative Evaluation and Preparation

1) Traditional treatment: is **dietary protein restriction** based on the presumption that a low-protein diet results in decreased protein catabolism and urea production (the serum urea is related to the severity of the clinical picture).

2) Preoperative Dialysis: (in anesthetic management of renal failure)
The **ideal time** of dialysis is on the day of surgery or the previous day. A common recommendation is that the **serum K^+ concentration** should be **less than 5.5 mmol/L** on the day of surgery.

Indications of Dialysis (Criteria of Inadequate Hemodialysis):
1- Laboratory:
- Creatinine clearance < 5 mL/min.
- Serum creatinine > 10 mg/dL (i.e., azotemia even in absence of uremia).
- Serum urea > 200 mg/dL (i.e., uremia).
- Serum K^+ > 7 mEq/L.
- Serum bicarbonate < 12 mEq/L.
- Serum albumin < 4 g/dL.

Inadequate hemodialysis is also indicated by:
- Persistent anemia (hematocrit < 30%) despite erythropoietin therapy.
- A decrease in BUN during hemodialysis < 65%.

- Pre-dialysis blood urea concentration < 50 mg/dL (a sign of malnutrition).
- Pre-dialysis serum creatinine concentration < 5 mg/dL (a sign of malnutrition).

2- Deterioration of the clinical picture: as
- Fluid overload (to remove excess volume to attain "dry weight") or ascites.
- Pericarditis.
- Refractory gastrointestinal symptoms as anorexia, nausea, or vomiting.
- Metabolic encephalopathy or depressed sensorium.
- Coagulopathy.
- Drug toxicity.
- Systemic hypertension.
- Poor nutritional status.

Avoid fluid overload or hypovolemia after dialysis. The patient's weight pre - and post-dialysis should be compared.

Serum electrolytes, BUN, and serum creatinine should be repeated to assess the adequacy of dialysis.

3) Examination of the Vascular Access:

• The patients with chronic renal failure usually have native arterio-venous fistulas (cephalic vein anastomosed to the radial artery). These fistulas may have complications such as infection, aneurysms, and ischemia of the arm.

• **Venipuncture (i.v. cannulas) and blood pressure measurement** should be avoided in the arm with arterio-venous fistula, even a Medic Alert bracelet should be worn for this.

• When dialysis is urgently required, vascular access is obtained with a double-lumen dialysis catheter, most often using the jugular or femoral vein.

4) Preoperative Detection and Management of Complications (and Clinical Pictures) of Renal Failure:

All systems should be assessed by history, examination and investigations such as:

1- **Cardiovascular System:**
- Proper management of heart failure, hypertension, arrhythmias, and heart block.
- Echocardiography to detect pericardial effusion and aspiration.
- ECG to detect arrhythmias, heart block, and ischemia.

2- **Pulmonary System:**
- Arterial blood gases to detect hypoxemia.
- Chest x-ray to detect pleural effusion, pericardial effusion, infection or pulmonary edema.

3- **Gastrointestinal Tract:**
- Preoperative fasting and proper premedication as there is an increased liability for aspiration.

4- **Endocrine System:**
- Serum glucose is done to detect hyperglycemia.

5- **Skeletal System:**
- Careful patient positioning as the patient is liable for bone fractures.

6- **Metabolic System:**
- Arterial blood gases to detect metabolic acidosis.
- Serum electrolytes to detect electrolyte disturbances.
  - Hyperkalemia may occur with metabolic acidosis. This causes ECG changes. Rapid correction is done by infusion of 80 mL of 50% glucose and 20 units soluble insulin. Adjust the dose according to the results. Long term correction is done by correction of metabolic acidosis by $NaHCO_3$ or ion exchange resin e.g., Ca^{++} polystyrene sulphate 15 g tid orally or retention enema 30 g. CaCl, or gluconate 10% 10-20 mL (0.5-1 g i.v. slowly) to antagonize the cardiac effects of K^+ with ECG monitoring.
  - Other electrolyte such as hypo -, hypernatremia…etc.

7- **Hematological System**:
- **Preoperative packed red blood cell transfusion** or **recombinant human erythropoietin** (*epoetin* or *darbepoetin*) transfusion to maintain hematocrit at 36-40% (its main side effect is hypertension). Both are indicated in
  - severely anemic patients (hemoglobin < 6 – 7 g/dL).
  - expected significant intraoperative blood loss.

Blood transfusions are better avoided if possible as the resultant sensitization by HLA antigens makes kidney transplantation less successful.

• **Bleeding time and coagulation studies**: Increased bleeding time indicates platelet dysfunction which is treated by:

Drugs	Dose	Onset of Effect	Peak Effect	Duration of Effect	Remarks
Cryoprecipitate	10 units i.v. over 30 min	< 1 hour	4-12 hour	12-18 hour	It contains factor VIII (and von Willebrand factor)
Desmopressin (1-desamino-8-D-arginine vasopressin "DDAVP")	0.3 μg/kg i.v. over 20-30 min or sub-cutaneous	< 1 hour	2-4 hour	6-8 hour	It is the non-vasoconstrictive analogue of vasopressin. It stimulates endothelial release of VWF-VIII. Tachyphylaxis occurs due to depleted stores and takes 4-7 days to be restored
Conjugated Estrogen	0.6 mg/kg/ day i.v. for 5 days	6 hour	5-7 days	14 days	

8- **Treatment of any infection** e.g., chest infection …etc.

9- **Preoperative Detection and Management of Complications of Dialysis**:

For example: i.v. volume depletion, pulmonary hypoxemia, hypokalemia or hypoproteinemia, and patients with long history of hemodialysis may be carriers of hepatitis B or C; so, full precautions should be taken by all operative personnel.

5) Preoperative Drug Therapy:

- Carefully adjust the doses of drugs according to the degree of renal impairment (as discussed above).
- Antihypertensive agents should be continued till the time of surgery.
- Adjust the dose of insulin (human regular).

Premedication:

Intramuscular injections should be avoided due to possibility of uremic platelet dysfunction.

1- Sedatives:

Generally, the doses of sedatives should be decreased.

The doses of **benzodiazepines** (metabolized by the liver) should be **decreased** because:

- Hypoalbuminemia increases the duration of action.
- Diazepam is used cautiously due to accumulation of its active metabolite N-des-methyl diazepam which is excreted by the kidney.

The doses of promethazine (a sedative and antiemetic) (metabolized by liver) should be decreased because its neurological action is increased by azotemia.

2- Anticholinergics:

Atropine and glycopyrrolate are safe in premedication doses, but on repeated administration, accumulation of their active metabolites may occur.

Scopolamine's central nervous action is increased by azotemia.

3-Aspiration Prophylaxis: Doses should be decreased.

H_2 blockers are excreted mainly by the kidney; therefore, their doses should be decreased.

Metoclopramide is used to accelerate gastric emptying 10 mg orally or slowly i.v. It is partially excreted by the kidney.

Intraoperative Management:

Monitoring:

Besides the standard monitors,

- **Blood pressure** (cuff or intra-arterial catheter) measurement: **It is avoided in the arm with the arterio-venous fistula** because the arterial pressure and the arterial blood gases will be inaccurate.
- **Invasive arterial blood pressure, central venous pressure, and pulmonary artery pressure:** They are used if major fluid shift is expected with **strict asepsis**. All catheters should be **re-heparinized** and sealed again especially after usage.

No site is the best for invasive blood pressure in chronic renal failure patient because:

- Radial, ulnar, brachial, and even axillary arteries should be avoided in any patient with chronic renal failure as they may be needed for an arterio-venous fistula in the future.
- Femoral arteries carry the risk of line infection, particularly because these patients may be immuno-compromised as a part of their disease process or due to therapy.
- Dorsalis pedis or posterior tibial arteries may be difficult to access due to edema and tissue indurations.

• **Do not place a urinary catheter** in anuric or oliguric chronic renal failure patient because it serves simply as a route for ascending infection.

Patient Position:

Extra padding is required to protect vulnerable nerves around elbows, knees, and ankles **and protect fistulas** to prevent pressure injury. If it is at all possible, the arm with the fistula should not be tucked, but positioned so that the **fistula thrill can be checked at intervals** throughout the surgery.

Choice of Anesthesia:

A) Regional Anesthesia:

It is **preferred** in minor surgeries such as establishment of arterio-venous fistula for dialysis. Regional anesthesia as brachial plexus block for the upper limb is used because it causes vasodilation and abolishes vasoconstriction.

Disadvantages:

- Care for **coagulopathy** as it is a relative contraindication.
- An increased risk of hypotension due to autonomic neuropathy.
- Postoperatively, after cessation of sympathetic blockade, increased systemic vascular resistance occurs with possibility of pulmonary edema.

B) General Anesthesia:

Induction:

Rapid sequence crash induction with cricoid pressure is usually indicated due to presence of nausea, vomiting, gastrointestinal bleeding, increased gastric acidity, and delayed gastric emptying which increase the risk of aspiration.

Induction agents:

- **Thiopentone** dose should be **decreased** to 2-3 mg/kg or only a sleeping dose is given due to:
  - hypoalbuminemia which decreases protein binding and results in increased free drug.
  - acidosis which increases the non-ionized fraction of drug. This increases drug entry to the brain.
- **Etomidate** dose should be **decreased** to 0.2 mg/kg due to:
  - hypoalbuminemia which decreases protein binding and results in increased free drug.

N.B.: **Ketamine is avoided** due to:

- Its hypertensive action in hypertensive renal patients.
- Its active metabolites which will accumulate in renal impairment or failure.

The hypertensive (pressor) response to intubation should be **avoided** e.g., i.v. injection of lidocaine (see chapter of "Airway Management"), but if patients are hypovolemic, exaggerated hypotension may occur in response to induction agents.

Succinylcholine 1.5 mg/kg is used safely if serum K^+ is < 5 - 5.5 mEq/L at the time of induction (suxamethonium increases serum K^+ by up to 0.5 - 1 mEq/L). If serum K^+ is higher or is doubtful, a non-depolarizing muscle relaxant should be used instead such as rocuronium with keeping in mind, that uremia may induce slowing of gastric emptying.

Maintenance: $O_2 \pm N_2O$ + volatile agents + opioids + muscle relaxant + controlled ventilation.

N_2O: is used cautiously or not used at all in:

- patients with poor ventricular function.
- severely anemic patients (hemoglobin < 7 g/dL) to allow the use of 100% O_2.

Volatile Agents:

- Volatile agents are ideal for patients with renal failure because:
  - they do not depend on the kidney for elimination,
  - they can control blood pressure, and
  - they have minimal effects on renal blood flow.
- In chronic renal failure, patients have severe anemia (hemoglobin < 5 g/dL), thus there is an accelerated induction and emergence due to: decreased blood: gas partition coefficient and decreased minimal alveolar concentration (MAC).

- **Isoflurane** is **the drug of choice** as it has the least effects on cardiac output.
  Halothane is used safely, but may decrease renal blood flow.
  Enflurane is a poor choice (used cautiously) as it increases fluoride levels theoretically and may decrease renal blood flow.
  Methoxyflurane is contraindicated as it increases fluoride ion level markedly causing nephrotoxic effects.
  Sevoflurane is used with some precautions as it must be used **with fresh gas flow more than one L/min.** Inspite of its fluoride production or compound "A" production with soda lime, there is no evidence that patients with co-existing renal disease are at increased risk of renal dysfunction following administration of sevoflurane.

Opioids:

- **Fentanyl, sufentanil and alfentanil** are of **choice** as they are metabolized in the liver to **inactive metabolites.**
- **Morphine and pethidine** are used in **small doses or better avoided** as they are metabolized in the liver to **active metabolites** which may accumulate in renal impairment.

Total Intra-Venous Anesthesia (TIVA) with remifentanil, propofol, and cis-atracurium has been recommended for patients with end-stage renal failure.

Muscle Relaxants:

- **Atracurium, cis- atracurium, and mivacurium** are of **choice** as they are not excreted by the kidney, but laudanosine toxicity (a metabolite of atracurium and cis-atracurium excreted by the kidney) may occur.
- **Rocuronium and vecuronium** are used **safely** as only a small % of them is excreted by the kidney.
- **D- tubocurarine, pancuronium, and pipecuronium** are used **cautiously** with neuromuscular monitoring as a large % of them is excreted by the kidney.
- **Metocurine, alcuronium, gallamine, and doxacurium** are **avoided** as they are mainly excreted by the kidney.

Controlled Ventilation: is of **choice** because:

- It **prevents respiratory acidosis** which could occur with spontaneous ventilation under anesthesia. Spontaneous ventilation increases the preexisting metabolic acidosis resulting in severe cardiovascular depression and increased serum K^+.
- It also **prevents respiratory alkalosis** because respiratory alkalosis
  - can shift the oxy-Hb dissociation curve to the left,
  - can increase the preexisting hypocalcemia, and
  - can decrease the cerebral blood flow.

Reversal of Muscle Relaxants:

- Edrophonium (75%), neostigmine (50%), and pyridostigmine (75%) are mainly eliminated by the kidney; so, their half lives in patients with renal impairment are prolonged at least as much as any of the above muscle relaxants. Therefore, recurarization is not expected.
- Pyridostigmine is preferred to neostigmine due to its longer duration.
- Glycopyrrolate is preferred to atropine due to: its longer duration and less anti-muscarinic effects; therefore, it is suitable for patients with hypertension or coronary artery disease.

Intraoperative Fluid Management:

Amount:

Judicious fluid therapy is needed.

- **In renal impairment, avoid volume depletion** which may cause postoperative renal failure.
- **In renal failure (anuric patients or those on dialysis), avoid volume overload** which may cause post-operative pulmonary edema. The fluid is replaced as follows:
  - For insensible water loss, 5-10 mL/kg/day i.v. 5% glucose.
  - For urine output, replaced with the same amount by 0.45% sodium chloride.
  - For 3rd space loss, replaced with the balanced salt solution or 5% albumin solution.
  - For blood loss, packed red blood cell transfusion is used.

Type:

- Avoid glucose containing solutions due to the associated glucose intolerance.
- **Avoid K^+ containing solutions** as ringer or lactated ringer in patients with hyperkalemia or in anuric patients; so, the use of **normal saline** is of choice.

N.B.: **The use of diuretics:** Stimulation of urine output with osmotic (mannitol) or loop (furosemide) diuretics in the absence of adequate intravascular fluid volume replacement is discouraged because:

- The most likely etiology of oliguria is an inadequate circulatory fluid volume, which can also be further compromised by drug-induced diuresis.
- Administration of mannitol or furosemide predictably increases urine output; but there is no evidence of corresponding improvement in GFR.
- Intraoperative urine output has not been shown to be predictive of postoperative renal insufficiency after abdominal vascular surgery.

Postoperative Management:

Close observation is needed to detect:

1- Postoperative Renal Failure: (in patient with renal impairment).

It results in postoperative oliguria.

Cause: It occurs in patients with renal insufficiency i.e., creatinine clearance 25-40 mL/min especially with sepsis, after major surgery or trauma; when they are exposed to volume depletion intraoperatively.

Treatment: (= **Renal Protection**):

- Adequate hydration.
- Avoid hypotension.
- Maintain urine output (after adequate hydration).

They are discussed before in management of acute renal failure.

2- Postoperative Apnea and Hypoxia (Recurarization):

It should be early detected and managed.

3- Postoperative Hypertension with/without Pulmonary Edema:

It should be treated by vasodilators and diuretics. Hemodialysis is a useful treatment.

4- Postoperative Analgesia:

- In renal impairment, non-steroidal anti-inflammatory drugs should be avoided.
- In renal failure, caution should be exercised in the use of parenteral opioids because they may cause exaggerated central nervous and respiratory depression. Naloxone may be needed in those patients.

5- Patients on Hemodialysis:

Hemodialysis should be delayed for 1-2 days postoperatively if possible to avoid heparin-induced bleeding.

Perioperative and Intensive Care Oliguria

Definition:

Urine output is < 0.5 mL/kg/hour.

Causes:

1- Incorrect catheter placement (as in the vagina in females or the urethra in males), **kinking** and **disconnection** from the reservoir tubing are the **most common** causes intraoperatively or in intensive care.

2- All causes of **acute renal failure** (see above).

3- In abdominal or pelvic surgery:

- **Compression** of the bladder by a retractor.
- Unintentional **cystotomy** or bladder rupture.
- **Ligation or severing of one or both ureters.**
- **Trendelenburg (head down)** position.

Management:

1- Management is directed to **the possible cause** such as:

- At first, **assess the integrity of the urinary catheter.**
- **Evaluate renal function and perform urine analysis as before to detect prerenal or renal causes.**
- In abdominal or pelvic surgery, notify the surgeon to check position of retractors on the ureters or the urinary bladder.

2- Administer a fluid volume challenge with assessment of central venous pressure as during management of hypovolemic shock (see before the chapter of "Cardiovascular Disease").

Renal Replacement Therapy (RRT) Dialytic Therapy for Renal Failure

The aim of renal replacement therapy is the removal of uremic toxins and the correction of fluid, electrolyte and acid-base disturbances.

Indications of Renal Replacement Therapy

They are discussed above.

The process of Renal Replacement Therapy

RRT uses an artificial kidney to remove fluid (solvent) and substances dissolved in the blood (solute). This is achieved through the use of a semi-permeable membrane, on one side of which blood flows, and on the other side filtered material is removed (i.e., hemofiltrate). Several processes are used to produce the hemofiltrate, usually in combination (figure 16-11).

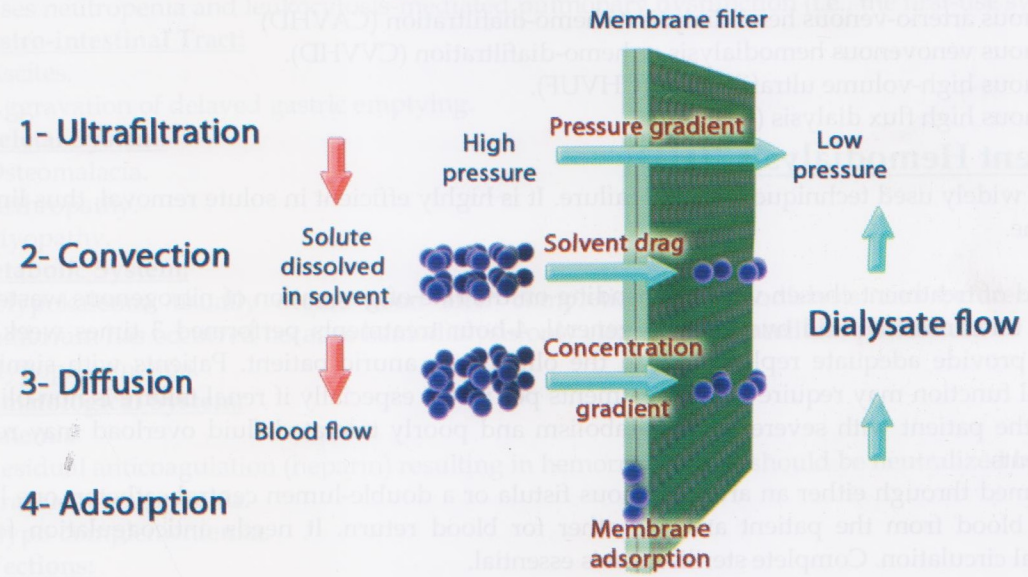


Figure 16-11: Processes of renal replacement therapy

1- Ultrafiltration:

As in the kidney, blood is pumped to a filtering membrane. The hydrostatic pressure is higher on the blood side of the filter than on the collection side, and fluid flows from the blood across the filter, leaving cellular material behind.

2- Convection:

During the process of ultrafiltration, dissolved material is carried across the membrane in response to the trans-membrane pressure gradient in a process known as "solvent drag". The rate of ultrafiltration and convection (hemofiltration) is determined by the porosity and the surface area of the membrane and the hydrostatic pressure of the blood, which depends on blood flow.

Hemofiltration is the principal mechanism for removal of water and middle-sized molecules (such as those responsible for uremia) from the blood.

3- Diffusion:

Diffusion is the movement of solutes from a component in which they are in high concentration to one in which they are in low concentration along an electrochemical gradient.

In hemodialysis, an electrolyte solution (dialysate) is pumped in a direction opposite (countercurrent) to the blood flowing on the other side of the semi-permeable membrane. This efficiently removes smaller molecules such as electrolytes, urea, and creatinine. Solute removal is directly proportional to dialysate flow rate.

4- Membrane Adsorption:

Artificial membranes (in particular AN69) have the capacity to adsorb solutes on their surface. This tendency is determined principally by pore size and surface area.

Types (and Modes) of Renal Replacement Therapy

a- Intermittent (last < 24 hours):

- Intermittent hemodialysis (IHD): is the main method used.
- Sustained low-efficiency dialysis (SLED).
- Extended daily dialysis (EDD)

b- Intermittent and Continuous:

- Peritoneal dialysis (PD).

c- Continuous:

- Continuous ambulatory peritoneal dialysis (CAPD).
- Continuous renal replacement therapies include:
  - Slow continuous ultrafiltration (SCUF).
  - Continuous arterio-venous hemofiltration (CAVH)
  - Continuous venovenous hemofiltration (CVVH).
  - Continuous arterio-venous hemodialysis or hemo-diafiltration (CAVHD)
  - Continuous venovenous hemodialysis or hemo-diafiltration (CVVHD).
  - Continuous high-volume ultrafiltration (CHVUF).
  - Continuous high flux dialysis (CHFD).

Intermittent Hemodialysis (IHD)

It is the most widely used technique for renal failure. It is highly efficient in solute removal, thus limiting treatment time.

Technique:

- The method of treatment chosen varies depending on the rate of generation of nitrogenous wastes and the patient's tolerance for fluid overload. In general, 4-hour treatments performed 3 times weekly are sufficient to provide adequate replacement in the oliguric or anuric patient. Patients with significant residual renal function may require fewer treatments per week, especially if renal failure is non-oliguric. Conversely, the patient with severe hyper-catabolism and poorly tolerated fluid overload may require daily treatments.
- It is performed through either an arterio-venous fistula or a double-lumen central catheter; one lumen for drawing blood from the patient and the other for blood return. It needs anticoagulation for the extracorporeal circulation. Complete sterilization is essential.
- IHD requires a pressurized, purified water supply, and has a greater risk of hemodynamic instability due to rapid fluid and osmotic shifts
- Blood is pumped into a filter, running countercurrent to dialysate (ionized water), and clearance is principally by dialysis and ultrafiltration.
- The blood flow rate is 200-400 mL/min, the dialysate flow rate is 500 mL/min, and the filtration rate is between 300-3000 mL/hour with urea clearance of 150-250 mL/min. With this high flow and clearance rate, patients only require 3-4 hours of dialysis, 2-3 times a week, depending on the extent of their catabolism.
- A relatively slow type of hemodialysis is used in a low-efficiency mode. This **slow (sustained) low-efficiency dialysis (SLED)** treatment is applied from 8-18 hours at a time and allows for less aggressive fluid removal. Also **extended daily dialysis (EDD)** is used all through the day with very slow dialysis. Both SLED and EDD are designed for critically ill patients because they are associated with fewer complications.
- **High flux dialysis** provides the most rapid solute clearance, but their use requires dialysis equipment with volumetric control of fluid removal.

Complications of IHD:

1- Central Nervous System:

- **Dialysis disequilibrium syndrome** (DDS): It causes hypotension (in 20-30% of patients), headache, nausea, vomiting, muscle twitches, fits, and coma. It is usually transient and resolves within hours due to rapid removal of urea from extracellular compartment causing more rapid decrease in extracellular compartment osmolality than intracellular compartment osmolality which increases the relative osmolarity of the brain and results in acute cerebral edema. To decrease the risk; short, gentle treatments (blood flows < 200 mL/min) should be prescribed until urea levels approach 100 mg/dL.
- Depression.
- Dementia.

2- Cardiovascular System:

- Rapid fluid removal may be poorly tolerated in some patients.
- Intravascular volume depletion.
- Hypotension due to ▫ vasodilation of acetate dialysate solution,
  ▫ the relative bio-incompatibility of cellophane or cellulose-based membranes that can cause enhanced activation of complement (is called the first-use syndrome) (see later),
  ▫ reactions to polyacrylonitrile (see later),
  ▫ autonomic neuropathy, and
  ▫ volume depletion.
- Myocardial ischemia or arrhythmias (which may accentuate the hypotension).

3- Respiratory System:

- Hypoxemia due to interaction of white blood cells with cellophane-derived dialysis membrane. This causes neutropenia and leukocytosis-mediated pulmonary dysfunction (i.e., the first-use syndrome).

4- Gastro-intestinal Tract:

- Ascites.
- Aggravation of delayed gastric emptying.

5- Skeletal System:

- Osteomalacia.
- Arthropathy.
- Myopathy.

6- Metabolic System:

- Hypokalemia usually occurs soon after completion of hemodialysis and before trans-cellular equilibrium has occurred because hemodialysis only clears the extracellular potassium.
- Hypoproteinemia.

7- Hematological System:

- Anemia.
- Residual anticoagulation (heparin) resulting in hemorrhage, and should be neutralized by protamine.
- Transient neutropenia.
- Hypo-complementemia.

8- Infections:

- Peritonitis.
- Transfusion related hepatitis (B and C) and acquired immunodeficiency virus (AIDS).

9- Hypersensitivity Reactions to the **ethylene oxide** used to sterilize the dialysis machine may occur as an adverse reaction to the specific membrane material, **polyacrylonitrile**. Reactions to polyacrylonitrile occur most commonly in patients receiving angiotensin-converting enzyme (ACE) inhibitors. When blood comes in contact with the polyacrylonitrile membrane, the membrane's high negative surface charge stabilizes enzymes which generate bradykinins. Normally, bradykinins are degraded by kinases, but ACE inhibitors block this response, and profound peripheral vasodilation and hypotension may occur.

10- Clearance and Removal of Drugs: Hemodialysis causes clearance and removal of drugs administered to the patient especially drugs with low molecular weight (< 500 Dalton), water-soluble, non-protein-bound drugs; therefore, these drugs should be re-administered after completion of hemodialysis.

Peritoneal Dialysis

Technique:

- It requires sterile placement of an anchored plastic catheter (either temporary or permanent) in the peritoneal cavity under local anesthesia for infusion of a dialysis solution. The most common approach is through a small midline incision 1 cm below the umbilicus.
- The peritoneal dialysate (dialysis solution) is a sterile balanced electrolyte solution with glucose but without potassium.
- The warm dialysis solution is infused into the peritoneum in a volume of 1-2 liters at a time. During the acute phase, fluid is drained continuously (i.e., with no dwell time). Once biochemical control is achieved, it is usual to leave fluid in place for 4-6 hours before drainage (dwell time is the time during which dialysate is allowed to stay in the peritoneal cavity). During that time, diffusive solute transport occurs across the peritoneal membrane until fresh fluid is exchanged for the old fluid i.e., the peritoneum acts as a semi-permeable membrane.

• Peritoneal dialysis patients undergoing abdominal surgery should have their dialysate drained prior to surgery for optimizing respiratory function. 24-48 hour of dialysis can be omitted, but they will need a short period of hemodialysis by a venous dialysis catheter.

Continuous Ambulatory Peritoneal Dialysis (CAPD)

• Patients undergo several automated peritoneal dialysis exchanges overnight. The night exchange is done by a mechanized cycler machine that is attached to the peritoneal dialysis catheter. It infuses and drains peritoneal dialysate 3 or more times at night. During the day, the patient may perform one or more manual exchanges to achieve an adequate dialysis dose. It allows more patient comfort.

Advantages of PD:

• Simple and does not need a vascular access.
• Cost-effective.
• No anticoagulation is required.
• In patients with diabetes, insulin can be infused with the dialysate with resultant precise regulation of blood glucose concentration.

Indications:

• It is preferred to hemodialysis in patients with congestive heart failure or unstable angina who may not tolerate the rapid fluid shifts or systemic blood pressure changes that may accompany hemodialysis.
• Patients with extensive vascular disease that prevents placing a catheter for vascular access.

Contraindications:

• Presence of abdominal hernias or adhesions may interfere with the ability to use peritoneal dialysis effectively.

Complications (Disadvantages):

• Peritonitis presented as abdominal pain, nausea, cloudy dialysate effluent, and fever, treated by antibiotics as cephalosporins, aminoglycosides, and vancomycin (i.v. or added to the peritoneal fluid).
• Poor solute clearance.
• Poor uremic control.
• Fluid leak with poor drainage.
• Catheter blockage due to bleeding.
• Hyperglycemia due to substantial glucose absorption (present in dialysate fluid) which needs intra-peritoneal insulin (5-10 units per 2-L dialysate bag).
• Diaphragm splinting which may cause pulmonary insufficiency.

Continuous Renal Replacement Therapies (CRRT)

• They are used usually in **critically ill patients** with acute renal failure who are hemodynamically unstable and are with hyper-catabolic states that require aggressive removal of solute **over 24-hour period** without major osmolar shifts. They are either:
  ▫ **Hemofiltration/ultrafiltration** for correction of **volume overload, uremia, and cytokine removal**.
  ▫ **Dialysis** for correction of **electrolyte and acid-base imbalance**.
  ▫ **Hemodialysis (Hemo-diafiltration)** i.e., **hemofiltration and dialysis**.
• **The dialysate and replacement solutions** should mirror the desired blood chemistry. Initially, a dialysate low in intracellular ions (potassium, magnesium, and phosphate) is used. Later on, when potassium is < 4.5 mEq/L, it is changed to a normokalemic solution.
• CRRT is either:
  ▫ blood pressure-driven (such as CAVH and CAVHD) i.e., CRRT is connected to both artery and vein and the patient's blood pressure is used to drive blood through the hemofilter. The most widely used is the combined cannulation of the femoral artery and vein, or
  ▫ pump-driven (such as CVVH and CVVHD) i.e., connected to a vein by a 10-12 Fr double-lumen central venous catheter where the blood is pumped through the hemofilter by a pump. Pump-driven CRRT is more preferable as it does not depend on the patient's blood pressure and the pump system incorporates alarms and safety features.

Indications:

• Azotemia (uremia).
• Hyperkalemia.
• Anuria/oliguria to make space for nutrition.
• Severe metabolic acidosis of non-tissue hypoperfusion origin.
• Fluid overload.

- Drug removal
- Hypothermia/hyperthermia.

Advantages of CRRT over Intermittent Dialytic Techniques:

1- Treatment is continuous, allowing for a constant readjustment of fluid and electrolyte therapy and the administration of large amounts of parenteral nutrition without the risk of interdialytic volume overload.

2- Especially in the hemofiltration-based treatments, convective mode of solute transport is used which increases middle-molecule clearance compared with diffusion-based dialytic techniques.

3- When compared with peritoneal dialysis, CRRT is not contraindicated in patients with prior abdominal surgery and offers isovolumetric fluid removal without the risk of peritonitis.

Disadvantages (and Complications) of CRRT:

1- Continuous anticoagulation by heparin is needed to prevent clotting of the filter (see its side effects such as hemorrhage at vascular access sites, peptic ulcers). Other drugs can be used instead of heparin such as prostaglandins E_1 and I_2, citrate (binds Ca^{++}), low molecular weight heparin, hirudin, or argatroban.

2- The patient must remain bedridden during the treatment.

3- Disconnection leading to hemorrhage.

4- Infection risk (sterile techniques must be employed).

5- Electrolyte, acid-base or fluid imbalance (due to excess input or removal).

They include:

1- Slow Continuous Ultrafiltration (SCUF):

It is used mainly for slow removal of fluid overload when aggressive fluid removal is intolerant e.g., congestive heart failure, during balloon pumping or during open-heart surgery. SCUF is insufficient for adequate solute removal.

Intermittent hemodialysis and slow continuous ultrafiltration (IHD + SCUF) may be combined together.

2- Continuous Arterio-venous Hemofiltration (CAVH):

The standard CAVH circuit allows blood to flow from an arterial access through a tubing circuit to a low-resistance hemofilter and back to a venous access. Filtrate which is relatively protein-free is collected into a bag connected to the ultrafiltrate port of the filter. Replacement fluid is infused into the venous tubing. Continuous anticoagulation is needed during the procedure.

3- Continuous Venovenous Hemofiltration (CVVH):

It avoids complications of arterial access. It is used for removal of fluid and has a convection-based clearance which increases middle-sized molecule clearance.

4- Continuous Arterio-venous Hemodialysis or Hemo-diafiltration (CAVHD):

The circuit is essentially the same as that for CAVH, but with the addition of a constant infusion of dialysate passing through the filtrate compartment of the filter. The blood flow rates are slow while the dialysate flow rate is high allowing efficient urea and solute clearance; therefore, this technique can be used in certain intoxications.

5- Continuous Venovenous Hemodialysis or Hemo-diafiltration (CVVHD):

It is the most popular method of dialysis in the intensive care units (both dialysis and ultrafiltration).There is continuous diffusive dialysis where the dialysate passes in a direction countercurrent to the blood allowing the maximum clearance capabilities of any continuous therapies especially for small molecule clearance (e.g., urea)

6- Continuous High-Volume Ultrafiltration (CHVUF):

Large amounts of fluid can be removed and replaced per hour as a means of cleaning the plasma e.g., to remove inflammatory cytokines. Ultrafiltration has very high rate and volume.

7- Continuous High Flux Dialysis (CHFD).

Anesthesia for Intensive Care Patients undergoing Continuous Renal Replacement Therapy

Indications:
- Surgical wound debridement.
- Tunneled dialysis catheter placement.
- Laparotomy.

Precautions and Managements:

- Continuous renal replacement therapy (CRRT) is **discontinued for the duration of the operating room visit**. Although it is theoretically possible to continue CRRT intraoperatively, but CRRT machines

are very difficult to be transported to operating room because fluid removal volumes are determined by weight; so, any movement during transportation upsets this process.

- **Continuous anticoagulation** is usually an unwanted perioperative hazard.
- Anesthesiologists should **avoid using the dialysis catheter for intraoperative access**. If there is no alternative, **heparin that is placed in both lumens of the line to prevent clotting** while disconnected from the CRRT machine should be withdrawn.

Plasma Exchange

Plasma exchange may be used to remove circulating toxins or to replace missing plasma factors.

Indications:

1- Autoimmune diseases: to remove unwanted antibodies.

- Goodpasture's syndrome.
- Guillain-Barré syndrome.
- Rapidly progressive glomerulonephritis.
- Myasthenia gravis
- Systemic lupus erythematosus.
- Thrombotic thrombocytopenic purpura.

2- Immuno-proliferative diseases:

- Multiple myeloma.
- Waldenstrom's macroglobulinemia.

3- Poisoning: • Paraquat.

4- Others: • Meningococcemia (possible benefit).

- Sepsis.
- Reye's syndrome.

Techniques:

Most diseases require a daily 3-4 L plasma exchange repeated for at least 4 further occasions over 5-10 days.

Cell Separation by Centrifugation:

Blood is separated into components in a centrifuge. Plasma (or other specific blood components) is discarded and a plasma replacement fluid is infused in equal volume.

Membrane Filtration

Plasma is continuously filtered through a large pore filter (molecular weight cut-off typically 1,000,000 Dalton). Plasma is discarded and replaced by infusion of an equal volume of replacement fluid. The technique is similar to hemofiltration and uses the same equipment.

Complications:

- Circulatory instability: due to intravascular volume changes, removal of circulating catecholamines, or hypocalcemia.
- Reduced cardiac output if replacement is with crystalloids.
- Infection.
- Bleeding due to removal of coagulation factors.

Intensive Care Considerations in Patient with Renal Failure

1- **Management (diagnosis and treatment) of comorbid conditions** such as neurological, cardiovascular, pulmonary, and gastrointestinal diseases should be applied by the usual way.

2- **Indications and complications of dialysis** and ultrafiltration therapies should be assessed and managed such as fluid removal for pulmonary edema or severe hypertension.

3- **Drugs** should be adjusted as regards the dosage and intervals according to the creatinine clearance and the effect of hemodialysis.

4- **Fluid management of a patient on dialysis**: Normal fluid restriction for a patient receiving maintenance hemodialysis (3 times weekly) often depends on the patient's tolerance for aggressive fluid removal during each treatment. **In general, fluid should be restricted to 1-1.5 L/day** and is dictated by the patient's tendency to develop hypertension or pulmonary congestion in the inter-dialysis period. A restriction of fluid intake to 1.5-2.0 L/day is often **well tolerated**, and that amount is easily removed with the ongoing dialysis.

5- **Nitrogen balance and caloric requirements:**

• Nitrogen balance studies in hemodialysis patients suggest that protein requirements are between 1 and 1.2 g/kg/day. Patients receiving chronic ambulatory peritoneal dialysis lose a substantial amount of protein in the dialysate (approximately 10 g/day), and their protein requirement approaches 1.4 g/kg/day.

• The caloric requirement to maintain neutral nitrogen balance is 37 kcal/kg/day.

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GENITOURINARY DISEASES

17

• Cystoscopy • The transurethral resection of the prostate (TURP) • Radical surgery for urologic malignancies Urinary bladder cancer Renal cancer Prostatic cancer Testicular cancer	• Extracorporeal shock wave lithotripsy (ESWL) • Organ transplantation • Renal Transplantation • Anesthesia for renal transplant recipients undergoing other surgery

Cystoscopy

Anesthetic Problems

1- Type of patients.
2- Lithotomy position.
3- Day case anesthesia.

Preoperative Management:

The Type of Patients: Most patients have:

• **Renal diseases**: They should be detected and managed as before.

• **Repeated rechecking for recurrence of bladder tumors**; so, the patient may be attending as **frequent** as every 6 months. Therefore, ▫ the patients may be relaxed due to multiple previous attendances.

▫ careful inspection of the anesthetic notes must be done to avoid unexpected problems. Just because a patient has been well 6 months ago does not mean that the same applies now.

Intraoperative Management:

Patient Position: **Lithotomy position** is used. Its technique, complications and precautions are discussed later.

Choice of Anesthesia:

A- General Anesthesia: It is usually **preferred** because:

- Most cases are usually short procedures (15-20 min).
- Most cases are day-case that need early recovery; therefore, propofol is preferred.
- General anesthesia is suitable for children.

B- Regional Anesthesia:

1- **Epidural or Subarachnoid Anesthesia**: It needs **T_{10} sensory level**.

• The sensory level should be well established (fixed before the patient is moved to the lithotomy position to avoid producing a higher level (actually this is a controversy).

• Regional anesthesia does not abolish the obturator reflex (external rotation and adduction of the thigh secondary to stimulation of the obturator nerve by electrocautery current through the lateral bladder wall). The reflex (muscle contraction) is reliably blocked only by muscle paralysis during general anesthesia.

• Spinal anesthesia is preferred due to its rapid onset.

2- **Topical Anesthesia**: By using viscous lidocaine with/without sedation can be used in most women due to their short urethra.

Penile Erection may occur due to:

- surgical stimulation when the depth of general anesthesia is inadequate or
- neuraxial block (epidural, spinal, or caudal).

Penile erection makes cystoscopy difficult. Penile erection can be managed by deepening anesthesia. If erection still persists, small doses of ketamine can be useful.

The Transurethral Resection of the Prostate (TURP)

Benign prostate hyperplasia is a nonmalignant enlargement of the prostate due to excessive cellular growth of both the glandular and stromal elements of the gland. TURP (and open prostatectomy) is the main treatment.

Anesthetic Problems:

1- Type of patients.
2- Lithotomy position.
3- Hemorrhage.
4- TURP syndrome.
5- Hypothermia.
6- Bladder perforation.
7- Coagulopathy.
8- Postoperative pain.
9- Postoperative septicemia.

Preoperative Management:

Type of Patients: Patients are **elderly** males with coexisting cardiac, pulmonary, and renal diseases (due to long standing urinary obstruction). The mortality rate with TURP is 0.5-0.6%. Common causes of death are:
- Heart infarction.
- Pulmonary edema.
- Renal failure.

Cross-matched blood should be available for anemic patients and those with large prostate size (>30-40 g).

Intraoperative Management:

Patient Position: **Lithotomy position.**

It is the 2nd most common used position after supine position.

Preoperatively: It is important to ensure that:
- There is no limitation of movement of these joints especially if there is osteoarthritis which is common in the elder patients.
- Preexisting lumbar back pain may be worsened by extended periods in this position; therefore, small lumbar support may be used to maintain the lumbar lordosis.

During positioning:
- Two personnel are required to safely move the patient's legs simultaneously up or down to avoid stressing the spinal ligaments.
- The assistants pull the patient down the table before elevating the legs.
- The hips are flexed 80 to 100 degrees from the trunk and the legs are abducted 30 to 45 degrees from the midline. The knees are flexed until the legs are parallel to the torso, and the legs are held in this configuration with stirrups (strap, bier-Hoff, or Allen). The strap supports should be padded and the legs should hang freely within the straps.
- The anesthesiologist should support the patient's head carefully and ensure that there is sufficient slack in the hoses of the breathing system to avoid accidental extubation or disconnection.
- The arms should be supported as they may fall from the table when the patient is moved.
- The sacrum should be supported (figure 17-1).



Strap (candy cane) stirrups Bier-Hoff stirrups Allen stirrups

Figure 17-1: Lithotomy position

Risks of Lithotomy Position:

1- Iatrogenic Injuries:

• Injury of **the common peroneal nerve** (resulting in loss of dorsi-flexion of the foot) due to compression by the strap supports against the lateral head of the fibula. The injury is more common in patients who have a low body mass index, recent cigarette smoking, or prolonged duration of surgery (> 2 hours).

• Injury of **the saphenous nerve** (resulting in numbness along the medial calf) due to pressure on the medial aspect of the leg which is resting on the strap support.

• Injury of the **obturator or femoral nerves** due to excessive flexion of the thigh against the groin.

• The normal lordotic curvature of the lumbar spine is lost, thereby potentially aggravating any previous lower back pain.

2- Respiratory Effects:

• It decreases vital capacity and functional residual capacity because abdominal contents restrict the movement of the diaphragm especially in the obese and elderly resulting in atelectasis and hypoxia which are accentuated by the head-down (trendelenburg) position. Therefore, O_2 saturation monitoring is essential.

3- Cardiovascular Effects:

• Leg elevation increases venous return acutely (adds about 600 mL blood to the central circulation). This precipitates or exacerbates congestive heart failure in a patient with a compromised heart.

• Also, rapid leg lowering decreases the venous return acutely resulting in hypotension and decreasing cardiac output especially with general anesthesia or regional anesthesia. Therefore, blood pressure monitoring is essential and the body position must be changed gradually.

• When a large abdominal mass is present (e.g., tumor or gravid uterus), leg elevation may increase abdominal pressure sufficiently to obstruct venous return to the heart.

Monitoring:

Besides the standard monitors,

- **Mental status** monitoring in awake patients is the best monitor for detection of early signs of TURP syndrome and bladder perforation.
- **Temperature monitoring:** is essential to detect hypothermia.
- **Clinical signs of hyper - or hypovolemia** should be observed.

Choice of Anesthesia:

A) Spinal or Epidural Anesthesia: It needs **T_{10} sensory level** block. It is of choice because:

- **It decreases surgical blood loss** by reducing blood pressure during surgery.
- It produces **vasodilation** which results in peripheral pooling of blood. This decreases the **severity of the circulatory overload**.
- It allows **early diagnosis of TURP syndrome** or bladder perforation in awake patients.
- **It decreases the incidence of postoperative venous thrombosis**.
- It allows postoperative analgesia.

Precautions:

- **Large i.v. fluid** preload **should be avoided** which may increase the risk of TURP syndrome.
- If hypotension occurs due to the neuraxial block, it is better treated by vasopressors e.g., **ephedrine than by i.v. fluids.**
- Sympathetic block causes vasodilation in the lower limbs. This increases vascular venous volume without an increase in the venous return to the heart, but **when the block dissipates**, venous capacity acutely decreases resulting in **circulatory overload**.
- In patients with cancer especially those with back pain, consider the possibility of **vertebral metastasis** as it is a contraindication of regional anesthesia.
- Recent studies have suggested that the incidence of **post-spinal headache** after TURP surgery is higher than had been suspected previously; so, the use of small gauge needles e.g., 26 is recommended.

B) General Anesthesia:

The best technique is by intubation and controlled ventilation with the following precautions:

- Avoid high airway pressures as they may increase bleeding form the prostatic bed.
- TURP syndrome may delay or prevent emergence from general anesthesia.

Intraoperative Fluid Management:

Amounts: **Minimal amounts** of fluid should be given to avoid circulatory overload.

Types: • **Na containing crystalloids** are preferred to decrease the risk of hyponatremia (see later).

- If blood transfusion is needed, packed red blood cells are preferred to avoid hypervolemia (see later).

Intraoperative Complications:

1) TURP Syndrome:

Causes: **Systemic absorption** of the irrigating fluid (especially if water is used) via:

- The opened extensive network of **venous sinuses** in the prostate.
- Fluid accumulation in the peri-prostatic and retro-peritoneal space if the prostate capsule is violated (opened) during surgery.

Factors Increasing the Incidence of TURP Syndrome:

The amounts of irrigating solution absorbed are increased by:

1- Prolongation of the **duration of resection** > 150 min. This increases morbidity and mortality (the usual procedure time is 45-60 min).

2- An increase **in the hydrostatic pressure of the irrigation fluid** determined by the height of irrigation fluid. After 60 -70 cm H_2O pressure (at 60-70 cm height above the patient), there is a marked increase in the absorption of irrigation fluids.

3- A decrease **in the venous pressure of the prostate**.

4- An increase in **the number and size of venous sinuses** opened during surgery determined by the size of the gland. Also violation of the capsule during surgery increases fluid absorption.

5- **The bad surgical technique**.

6- **Excessively distended bladder** during surgery.

Average Amount Absorbed:

It is **20 mL / min**. It is usually 1-1.5 L, but may be increased up to 5-8 liters. Volume absorbed can be calculated by the following equation:

$$\text{Volume absorbed} = \frac{\text{Preoperative serum } Na^+}{\text{Postoperative serum } Na^+} \times \text{ECF - ECF}$$

Provided that extracellular fluid (ECF) is 20-30% of body weight in kg.

For example: A 60 kg patient with preoperative serum Na^+ 140 mEq/L and postoperative serum Na^+ (or Na^+ at the time of assessment) 100 mEq/ L.

So; 140/100 ECF – ECF = 1.4 ECF – ECF = 0.4 ECF = 0.4 x 60 x 20% = 4.8 liters.

Types of Solutions Used:

a- **Isotonic or Near Isotonic (Slight Hypotonic) Non-Electrolyte Irrigating Solutions**:

- Glycine 1.2% and 1.5% (288 mOsm/L).
- Cytal (mixture of sorbitol 2.7% and mannitol 0.54%) (195 mOsm/L).
- Mannitol 3%.
- Sorbitol 3.3%.
- Dextrose (glucose) 2.5-4%.
- Urea 1%.

b- **Distilled Water**:

It is not used now because:

- It is an extremely hypotonic solution causing **hemolysis**.
- On significant absorption, **acute H_2O intoxication** may occur.

N.B.: Electrolyte solutions are avoided (not used) for irrigation in TURP because they can conduct the electrical current from the electrocautery (i.e., resectoscope) to the surrounding tissues causing burns.

Clinical Picture:

It can appear **intra-** or **post**operatively (from a few minutes after the onset of surgery up to hours after the end of surgery).

In **awake patients**, the 1st symptoms are difficult breathing, headache, nausea, vomiting, dizziness, or confusion.

In **anesthetized patients**, the 1st symptoms are increased blood pressure (then hypotension), decreased heart rate, increased airway pressure, or delayed recovery from anesthesia.

The following clinical picture occurs:

a- Dilutional Hyponatremia: (with any type of solutions)

The clinical picture appears when serum Na^+ reaches < 120 mEq/L such as:

• **Cerebral edema up to irreversible brain damage:** It causes loss of alpha waves with irregular discharge of high amplitude slow wave activity on electroencephalogram.

Actually, these neurological effects are not related to the degree of the fall of serum Na^+, but to the rate (speed) of the fall of serum Na^+ as more rapid fall in serum Na^+ results in increased neurological effects.

• **ECG changes:**

At 120 mEq/L: Possible widening of QRS complex occurs.

At 115 mEq/L: Widened QRS, elevated ST segment, inverted T wave, and U wave occur.

At 110 mEq/L: Premature ventricular contractions, ventricular tachycardia, ventricular fibrillation occur.

At 100 mEq/L: Cardiac arrest may occur.

• **Altered renal function** causing decreased postoperative urine output.

• It may prolong the non-depolarizing muscle relaxant actions.

b- **Hypo-osmolality (Acute Water Intoxication):** (if distilled water is used).

• **Cerebral edema** causes headache, restlessness, confusion, seizures, increased intracranial tension, decerebrate posture, dilated sluggish reactive pupils up to coma lasting for a few minutes up to days.

• **Hypotension and bradycardia**. Bradycardia is due to hypertension or increased intracranial tension.

• Acute intravascular **hemolysis** causes sudden prostrations, chills, clammy skin, tight chest, bronchospasm, increased serum K^+ (resulting in ventricular fibrillation). Free hemoglobin which reaches the renal tubules results in renal failure and shock.

c- **Fluid Overload:** (with any type of solutions)

• Congestive heart failure.

• Pulmonary edema.

Both cause dyspnea, cyanosis, and arrhythmias which result in angina.

• Increased blood pressure (then hypotension occurs).

d- **Solute Toxicity:**

1- **Hyper-glycinemia (i.e., Glycine Toxicity):**

Due to increased serum glycine > 1000 mg/L (normal = 13-17 mg/L).

Glycine is an inhibitory neurotransmitter so its toxicity results in:

• Central nervous toxicity (inhibition).

• Cardiovascular toxicity (depression): decreased cardiac output.

• Eye toxicity: blurring of vision, haloes around objects, or transient blindness which gradually resolves within 8-48 hours after surgery (due to the toxic effect of glycine on the retina).

• Renal toxicity and failure due to hypotension and hyperoxaluria (oxalic acid is a major metabolite of glycine).

• **Hyper-ammonemia**: (very rare) due to increased serum ammonia > 500 µmol/L (normal = 5-15 µmol/L) because ammonia is derived from glycine degradation. Ammonia produces central nervous toxicity as nausea, vomiting, and coma which resolve when the ammonia levels become < 150 µmol/L. It is suggested that **arginine deficiency** predisposes to the central nervous toxicity after absorption of glycine solution because the arginine is an intermediate in the conversion of ammonia to urea in the ornithine cycle in the liver. Therefore, addition of arginine or ornithine to glycine irrigating solutions may protect against hyper-ammonemia and hence central nervous toxicity.

2- **Hyperglycemia** due to increased sorbitol or dextrose especially in diabetic patients.

Management of TURP Syndrome:

a- **Prophylactic Measures**:

1. Preoperative correction of heart failure, fluid and electrolyte imbalances.
2. Avoid factors which increase the incidence of TURP syndrome such as decreasing the duration of the resection, avoiding elevation of fluid height > 60 cm, good surgical techniques, voiding the bladder, and maintaining the blood pressure.

b- **Therapeutic Measures**:

Early detection is very important. When TURP syndrome is suspected the following measures should be done:

1. **Notify the surgeon** to discontinue surgery as soon as possible.
2. **Restrict fluid** by slowing i.v. fluids.
3. Recheck serum electrolytes, hemoglobin concentration and arterial blood gases.

Once diagnosis is established:

1. **Diuretics** are given to eliminate the absorbed water e.g., furosemide 20 mg i.v or mannitol 0.5 g/kg i.v.

2. **Oxygen** mask or nasal cannula application is essential to eliminate hypoxia.
3. Treatment of symptomatic **hyponatremia** when serum Na^+ is < 120 mEq/L as follows:
   - In mild cases: Normal saline 0.9% is infused till serum Na^+ approaches the normal level.
   - In severe cases: hypertonic saline (3% or 5%) is used.
     - It should be given at a rate < 100 mL/hour to avoid circulatory fluid overload.
     - Serum Na^+ should be corrected at a rate < 0.5 mEq/L/hour (i.e., < 12 mEq/L/day) because **rapid correction** causes **central pontine myelinolysis (osmotic demyelination syndrome)**.
     - 300 mL of hypertonic saline can usually correct the hyponatremia.
4. Treatment of **Seizures** by: midazolam 2-10 mg i.v.,
   diazepam 5-20 mg i.v.,
   thiopentone 50-100 mg i.v., or
   phenytoin 10 -20 mg/kg.
5. **If pulmonary or cerebral edema** occur, they are treated by:
   - **Intensive care** admission and **invasive monitoring** such as invasive blood pressure, central venous pressure, and pulmonary artery pressure.
   - **Endotracheal intubation** and **mechanical ventilation** to prevent aspiration in deteriorated level of consciousness.
   - **Dehydrating measures**.

2) Increased Blood Loss (Hemorrhage):

Generally, blood loss is related to the surgical experience, the duration of the procedure, and the size of the prostate. In TURP, blood loss is increased **due to associated coagulopathies** (see later).

Blood loss is **often difficult to assess** because the blood is heavily diluted by the irrigating fluid and an inexperienced anesthesiologist often underestimates the total losses. Therefore, the anesthesiologists **should depend on clinical signs.**

3) Coagulopathy:

Causes:

1. **Disseminated intravascular coagulopathy (DIC)** due to the release of thromboplastin from the prostate into the circulation.
2. **Dilutional thrombocytopenia** as a part of TURP syndrome.
3. **Primary fibrinolysis** in patients with metastatic carcinoma of the prostate because the tumor is thought to secrete a fibrinolytic enzyme.
4. **Release of fibrinolytic agents** (plasminogen and urokinase) from the mucosa of the lower urinary tract.

Clinical Picture and Investigations:

- Diffuse uncontrollable bleeding.
- Coagulation profile shows decreased platelet count, decreased fibrinogen, and increased fibrin degradation products (FDPs).

Treatment:

- For DIC: Platelets, cryoprecipitate, FFP, and heparin (controversial) are used.
- Consultation of a hematologist is beneficial.

4) Intraoperative Hypothermia:

Irrigation solutions given at room temperature decrease the body temperature 1°C per hour resulting in hypothermia which occurs in 5% of patients; therefore, irrigating solutions should be warmed to body temperature.

5) Bladder Perforation:

Incidence: 1% in TURP.

Causes:
- Resectoscope.
- Over-distension of the bladder with the irrigating fluid.
- Rarely, by explosion of traces of hydrogen gas inside the bladder by cautery.

Clinical picture: is either:

a- Extra-peritoneal manifested by:
- Poor return of the irrigating fluid as an early sign.
- Nausea, diaphoresis, and retropubic or lower abdominal pain in awake patients.

b- Intra-peritoneal (or large extra-peritoneal) manifested by:
- Sudden unexplained hypotension (may by hypertension with bradycardia, vagal mediated).

- Reflex movement of the limbs in awake patients anesthetized by regional or general anesthesia.
- Generalized abdominal pain and shoulder pain (due to diaphragmatic irritation) in awake patients.

Diagnosis is confirmed by cysto-urethrography.
Treatment: Immediate supra-pubic cystotomy.

Postoperative Management:

1) Postoperative Analgesia: is mandatory due to

- the old age of patients
- presence of urinary catheter that irritates the raw prostatic bed.

Analgesia is maintained by opioids (but decrease the dose in elderly) or by the epidural route.

2) Postoperative Septicemia:

It can occur because opening of the venous sinuses allows entry of organisms into the blood stream. This causes septicemia up to septic shock which usually lasts for a few hours and then the patient recovers from it. Prophylactic antibiotics (commonly gentamycin) are given preoperatively.

3) Continuous Bladder Irrigation:

It is important to prevent blood clotting in the catheter. The fluid used for irrigation should be:

- warmed to avoid postoperative hypothermia and shivering as this may dislodge the clots resulting in increased postoperative bleeding.
- checked regularly for its volume to ensure that large amounts are not being absorbed.

Q: What are the possible causes of hypotension during TURP?

Laser Prostatectomy

It is a new technique that may replace conventional TURP.

Technique:

The neodymium: yttrium-aluminum-garnet (Nd: YAG) laser, holmium laser, and potassium-titanyl-phosphate (KTP) laser are commonly used. These lasers produce variable degrees of coagulation and vaporization of prostate tissue.

Advantages: (over the conventional TURP)

- Minimal fluid absorption.
- Ability to use normal saline as an irrigating fluid (instead of a non-electrolyte solution as glycine). Both decrease TURP syndrome.
- Minimal blood loss (as little as 50-70 mL).

Disadvantages:

- Coagulation through the prostatic fossa and sloughing of prostatic debris in the postoperative period, with subsequent urinary obstruction and urinary retention.
- Protective eyewear should be used.
- The smoke plume of the laser should be removed.

Radical Surgery for Urologic Malignancies

A) Urinary Bladder Cancer: (Radical Cystectomy)

Anesthetic Problems:

1) Type of Patients:

Patients with carcinoma of the urinary bladder may be heavy **cigarette smokers** (as it is one of the risk factors); therefore, these patients may have coronary artery disease or chronic obstructive lung disease.
Patients with chronic obstructive uropathy have **renal impairment**.

2) Chemotherapy:

It is usually taken by these patients preoperatively and can cause:

- **Bone marrow depression.**
- **Renal impairment** by cisplastin.
- **Pulmonary fibrosis** by bleomycin.
- **Cardiomyopathy** by doxorubicin.
- **Neuropathy** by vincristine.

3) Increased Blood Loss:

Controlled hypotensive anesthesia is usually used.
Monitoring of urine output is important. Urinary pathway is interrupted at some point during most of these procedures.

Invasive monitoring such as invasive blood pressure, central venous pressure, and pulmonary artery pressure monitoring are needed.

4) Special Considerations:

a) Retro-Peritoneal Lymph Node Dissection:

- **Pulmonary fibrosis** (from bleomycin) may be present; the use of high O_2 concentrations, and excessive i.v. fluids may cause **postoperative adult respiratory distress syndrome;** so, adjust O_2 to keep the $SaO_2 > 90\%$ with positive end-expiratory pressure (PEEP).
- **Bone marrow depression** may be present in some patients; so, some anesthesiologists prefer air-O_2 mixture than N_2O-O_2.
- **Mannitol** is given just before dissection near the renal arteries to prevent ischemic renal injury from **surgically induced renal vasospasm** by preserving renal blood and tubular flow.
- **Ligation of intercostal arteries** during **left sided** dissection may rarely cause **paraplegia** because the arteria redicularis magna (artery of Adam Kiewicz) which is a branch from these left intercostal arteries will cause ischemia to the lower 1/2 of the spinal cord which is supplied by it.
- Aggressive postoperative analgesia to decrease the respiratory complications occurring after thoraco-abdominal incisions is essential e.g., continuous the epidural analgesia or intercostal nerve block.

b) Urinary Diversion:

It is implanting the ureters into a segment of bowel (ileal or colonic) that is made to function as a conduit or reservoir conducting urine from the ureters to outside the skin.

- Urine output monitor is important. During ureteric division, no urine output occurs. This may be misleading and may cause over-fluid administration.
- Regional anesthesia causes sympathetic block. This causes unopposed parasympathetic action leading to a much contracted, hyperactive bowel that makes the surgical technique very difficult. Therefore, the use of anticholinergics (glycopyrrolate 1 mg) or papaverine (50-100 mg as slow i.v. infusion) may treat this problem.
- Postoperatively, electrolyte imbalance occurs such as **hyperchloremic metabolic acidosis** and **hypokalemia** due to the following:

Cause (in ileal wall):

1. Na^+ is absorbed in exchange with K^+ (or H^+) ions resulting in K^+ loss causing hypokalemia.
2. Cl^- is absorbed in exchange with HCO_3^- (resulting in metabolic acidosis); so, when Cl^- reabsorption exceeds Na^+ reabsorption, hyperchloremic metabolic acidosis occurs (figure 17-2).

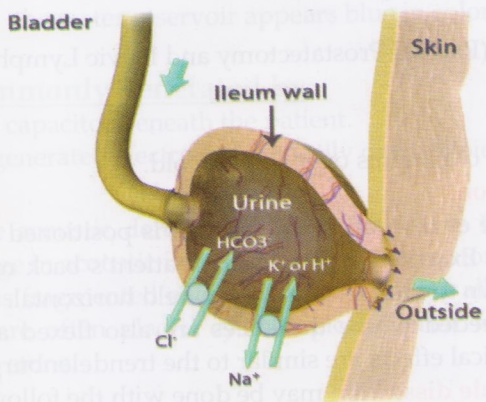


Figure 17-2: Urinary diversion

Factors increasing hyperchloremic metabolic acidosis:

1. Longer contact of urine with the bowel wall e.g., partial obstruction or redundancy of the conduit.
2. Hypovolemia.
3. Preexisting renal impairment as it impairs compensation for excessive HCO_3^- loss.

Treatment:

1. Treatment of the cause e.g., flushing the conduit with normal saline for partial obstruction and i.v. fluids infusion for hypovolemia.
2. Severe cases need i.v. $NaHCO_3 \pm K^+$ supplementation.

B) Renal Cancer: (Radical Nephrectomy)

Anesthetic Problems:

1) Type of patients:
They are usually 50-60 years old with elderly systemic diseases and smoking habits.

2) Position: **Modified lateral position with kidney rest** under the iliac crest. The table is hyper-extended to open the flank space and the upper arm is suspended above the patient.

3) Para-malignant syndrome may be present as erythrocytosis (i.e., increased hemoglobin), hypercalcemia, and hypertension.

4) General anesthesia is needed due to
- the length of the procedure.
- the patient's discomfort from the position.

5) Retraction of inferior vena cava may cause transient hypotension.

6) Increased blood loss which may need massive blood transfusion.

7) Pneumothorax may occur due to: opening of the pleura during surgery, or intercostal nerve block.

Although it may manifest up to 24 hours later, some authors insist on an immediate chest x-ray although it may not be helpful.

8) Tumor thrombus may extend into:
- Inferior vena cava, but below the liver (level I).
- Inferior vena cava up to the liver, but below the diaphragm i.e., hepatic vein (level II).

or • Above the diaphragm into the right atrium (level III).

These have the following implications:
- **Fatal pulmonary embolism** may occur.
- **Cardiopulmonary bypass** with hypothermia and heparinization may be needed if the tumor occupies > 40% of the right atrium. Hypothermic circulatory arrest may be needed.
- Complete inferior vena cava obstruction **increases blood loss** because it markedly dilates the venous collaterals. **Massive blood transfusion** is usually needed.
- **Central venous pressure and pulmonary artery pressure catheters** are used cautiously as they may dislodge the thrombus. Level III thrombus contraindicates pulmonary artery catheter. Central venous pressure is high due to inferior vena cava obstruction.
- **Trans-esophageal echocardiography** is useful to detect thrombus extension and the hemodynamic effects as hypotension and arrhythmias.

C) Prostatic Cancer: (Radical Prostatectomy and Pelvic Lymph Node Dissection)

Anesthetic Problems:

1) Type of patients:
Prostatic cancer is present in 75% of patients over 75 years old.

2) Hyper-extended supine position:
It is needed to facilitate exposure of the pelvis. The patient is positioned supine with the iliac crest over the break in the operating table. Excessive strain on the patient's back must be avoided. The operating room table is also tilted head-down to make the operative field horizontal.

The frog-leg position may be needed where the knees are also flexed and the hips are abducted and externally rotated. The physiological effects are similar to the trendelenburg position.

3) Laparoscopic pelvic lymph node dissection may be done with the following implications:
- A steep Trendelenburg position and rotation from side to side for surgical exposure are needed.
- There is a risk of CO_2 absorption from the retro-peritoneum.
- There is a risk of hypothermia from copious fluids used to irrigate clots from the pelvic fossa.

4) The surgeon may ask for i.v. indigo carmine dye for visualization of the ureters. This dye can cause **hypertension or hypotension.**

5) There is increased blood loss with its problems.

6) General anesthesia is usually needed.

7) There is increased incidence of deep venous thrombosis (DVT) because it is a pelvic surgery; thus its precautions should be taken.

D) Testicular Cancer: (Radical Orchiectomy and Retro-peritoneal Lymph Node Dissection)

Anesthetic Problems:

1) Type of patients:
They are usually young 15-35 years old.
2) Chemotherapy: as urinary cancer.
3) General or regional anesthesia is used.
4) Mannitol is given to protect kidney.
5) Retraction of inferior vena cava may cause transient hypotension.
6) Reflex bradycardia from retraction on the spermatic cord may occur.

Extracorporeal Shock Wave Lithotripsy (ESWL)

It is the use of focused **sound high-energy shock waves** that are applied to patients either:

- with the patient suspended in a water bath (in old models), or
- just via a reservoir of water over the patient's skin (in recent models) (figure 17-3).

It is a non-invasive technique.

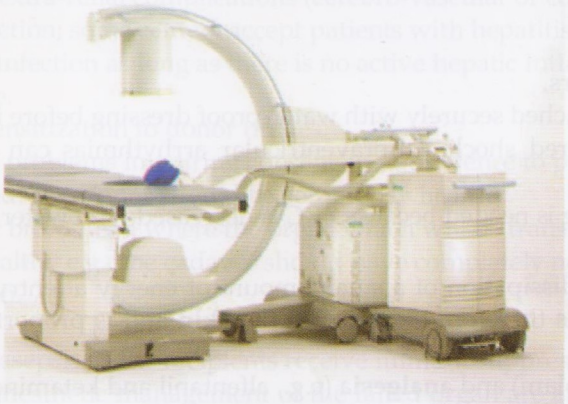


Figure 17-3: An extracorporeal shock wave lithotripsy; the water reservoir appears blue in color

Shock waves are most commonly generated by:

- Discharging an underwater capacitor beneath the patient.
- Recently, shock waves are generated electro-magnetically or from piezo-electric crystals.

Principles:

Because tissues have the same acoustic density as water, the waves travel through the body without damaging tissues, but the change in acoustic impedance at the tissue-stone interface creates shear and tear forces on the stone. The stone is fragmented enough by the waves to allow its passage down the urinary tract whereas ureteric stents are often placed cystoscopically prior to the procedure to facilitate the passage of large particles of the stone.

Contraindications:

1- Inability to position the patient to keep the lung and intestine away from the wave focus can cause tissue destruction at air-tissue interfaces.
2- Urinary tract obstruction below the stone.
3- Untreated infections.
4- Bleeding diathesis.
5- Pregnancy.
6- Presence of a nearby aortic aneurysm or orthopedic prosthetic device. Both are relative contra-indications in some centers.

Complications:

1- Ecchymosis, bruising, or blistering of the skin over the treatment site.
2- Large peri-nephric hematoma rarely.

Anesthetic Management:

Preoperative Management:

• Patients with history of cardiac **arrhythmias** and those with **pacemakers** are at risk of developing arrhythmias induced by the shock waves.

• Shock waves can damage the internal components of some pacemakers.

Therefore, **synchronization of the shock waves to the R wave from the ECG** decreases the risk of arrhythmia. The shock waves are usually timed to be 20 msec after the R wave to correspond to the ventricular refractory period.

Intraoperative Management:

In old models, the effects of immersion into a heated water bath (36-37°C) were as follows:

1- Initial and transient vasodilation resulting in hypotension.

2- Later on arterial blood pressure increases due to redistribution of venous blood centrally by the hydrostatic pressure of water on the legs and abdomen.

3- A sudden increase in venous return also occurs resulting in precipitation of congestive heart failure in patients with marginal cardiac reserve.

4- An increase in intra-thoracic blood volume results in decreased functional residual capacity (FRC) (30-60%). This predisposes to hypoxemia in patients with marginal pulmonary reserve.

In recent models, there is no need for the water bath immersion; only small amounts of water are placed in a reservoir on the skin.

Monitoring:

Besides the standard monitors,

• ECG pads should be attached securely with water-proof dressing before immersion (in old models). Even with R-wave triggered shocks, supraventricular arrhythmias can still occur and may require treatment.

• O_2 saturation monitoring is needed because FRC is decreased with water immersion.

Choice of Anesthesia:

Pain during ESWL is from dissipation of a small amount of energy at entry of shock waves to the body through the skin. The pain is therefore **localized to the skin** and is proportionate to the intensity of the shock waves.

a) I.v. Sedation (e.g., midazolam) and **analgesia** (e.g., alfentanil and ketamine) are usually enough.

b) Regional Anesthesia: in some centers.

• Regional anesthesia such as continuous **epidural** block, **spinal** block, or **intercostal** block with **local infiltration**. **T6 sensory level** block is needed because renal innervation is from T_{10}-L_2. Epidural fentanyl supplementation with 50-100 µg is often useful.

• As little air as possible should be used with the loss of resistance technique during insertion, as large amounts of air in the epidural space can dissipate the shock waves and theoretically may promote injury to neural tissues.

• Light sedation is usually needed for most patients. O_2 supplementation by face mask or nasal cannula should be done to avoid hypoxemia.

• Only in old models, i.v. fluid loading with 1000 mL of lactated ringer's solution is generally advisable before moving patients upright into the hydraulic chair to prevent postural hypotension.

Disadvantages:

1- Inability to control **diaphragmatic movement**: as excessive diaphragmatic excursions during spontaneous ventilation can move the stone in and out of the wave focus and may prolong the procedure. This problem can be partly solved by asking the patient to breathe in a more rapid, but shallow respiratory pattern.

2- **Bradycardia**: from high sympathetic blockade may prolong the procedure when shock waves are coupled to the ECG.

c) General Anesthesia:

• Light general anesthesia with intubation, a muscle relaxant, and controlled ventilation may be used. This allows the control of diaphragmatic movement.

• In old models, the procedure is risky as it is associated with placing a supine anesthetized patient in a chair, elevating and then lowering the chair into a water bath to shoulder depth, then reversing the sequence at the end.

d) EMLA Cream:

It can be applied over the skin at the site of the shock waves one hour before the procedure.

Fluid Management:

- I.v. fluid therapy is typically generous due to:
  - In old models, initial i.v. fluid loading is given as above.
  - Lactated ringer's 1000-2000 mL is usually given with a small dose of furosemide 10- 20 mg to maintain brisk urinary flow and flush stone debris and blood clots.
- Patients with poor cardiac reserve require more conservative fluid therapy.

Organ Transplantation

General Principles: in any organ transplantation.

1- Indications: End stage organ failure such as end stage renal failure in renal transplantation.

2- Recipients - have clinical pictures of the organ failure such as clinical picture of liver failure in liver transplantation.

- should have no contraindications such as:
  - Reversible organ impairment such as reversible renal impairment.
  - Ability of conservative measures to maintain a useful life.
  - Advanced extra-renal complications (cerebro-vascular or coronary diseases).
  - Active infection; some centers accept patients with hepatitis B, C, and immunodeficiency virus (HIV) infection as long as there is no active hepatic inflammation or cirrhosis.
  - Drug abuse.
  - Previous sensitization to donor tissues.
  - Psychiatric problems impairing consent and adherence to perioperative therapy.

3- The donor:
- Living-related: The donor should be completely healthy.
- Cadaveric or brain-dead where the organ which will be transplanted should be completely healthy e.g., the cadaver should have completely normal heart in heart transplantation.

4- Anesthetic Management:

- There must be complete asepsis as the recipients receive immunosuppressive drugs.
- The same principles of anesthetic management of the failed organ are applied to the recipient before organ transplantation such as avoiding muscle relaxants that depend on renal excretion in a recipient with renal failure.
- Immuno-suppressive drugs are given pre-, intra-, and post-operatively.
- Intraoperative graft assessment is performed e.g., urine output in renal grafts or bile formation in liver grafts.
- Postoperative management includes:
  - Intensive care admission.
  - Pain relief.
  - Complications such as:
    - Graft failure and its assessment such as liver failure that occurs postoperatively.
    - Rejections are: super-acute (that occurs intraoperatively),
      acute (hours to weeks), or
      chronic (months to years).
    - Complications due to arterial connection; vascular spasm or occlusion.
    - Complications due to venous connection; hemorrhage.
    - Complications of lymphatics e.g., lymphocele because lymphatics are not connected during surgery.
    - Complications due to lumen connection; a leak such as ureteric or biliary leak.
    - Infections due to immunosuppression.
    - Increased incidence of cancer due to chronic immuno-suppression.

The most common organ transplantations are renal, liver, pancreas, heart, and lung transplantation. They are discussed in their corresponding chapters.

Renal Transplantation

Indications: Patients with end stage renal failure on established programs of long-term hemodialysis. Causes of renal failure are discussed in the chapter of "Renal Diseases".

Contraindications:

a- Absolute Contraindications:

- **Reversible** renal impairment.
- **Ability of conservative measures** to maintain a useful life.
- Advanced forms of **major extra-renal complications** (cerebro-vascular or coronary disease, or neoplasia).
- **Active infection;** some centers accept patients with hepatitis B, C, or immunodeficiency virus (HIV) infection as long as there is no active hepatic inflammation or cirrhosis.
- **Active glomerulonephritis**.
- **Previous sensitization to donor tissues.**
- **Drug abuse.**

b- Relative Contraindications:

- Age **> 60** to 65 years.
- Presence of **vesical or urethral abnormalities**.
- **Ilio-femoral occlusive disease**.
- **Psychiatric** problems impairing consent and adherence to perioperative therapy.
- Oxalosis.
- Smoking.
- Morbid obesity.

Anesthetic Management:

Anesthetic Problems:

1- The transplanted kidney is either cadaveric or living related.
2- The recipient is a patient with end stage renal failure with its anesthetic problems.
3- Immunosuppressive drugs are given to the recipient.
4- Complete precautions against infections.
5- The graft preparation and anastomosis.
6- The graft adequacy.
7- Problems of clamp release.
8- Intraoperative fluid management.
9- Postoperative complications.

The Transplanted Kidney (Donor Graft)

There must be matching of both:

- **ABO groups**.
- **Tissue typing**: The human major histo-compatibility complex is a cluster of genes on chromosome 6 that encodes **human leukocyte antigens (HLA)**. Before any transplant, specific HLA antigens are identified in all donors and recipients. Outcome is the best with a perfect HLA matched donor and recipient. The kidney with the least number of mismatches is preferred. Again because of improvement in immunosuppression protocols, recipients can receive an organ from a donor with a less than perfect match.

The transplanted kidney is either:

a- A Cadaveric Graft: Current organ preservation techniques allow ample time **(24-48 hours)** to preserve a cadaveric kidney at low temperature, thus allowing ample time for preoperative recipient preparation e.g., dialysis.

or b- Living related graft: The donor should be completely healthy. Living related transplants are performed electively with the donor and recipient anesthetized simultaneously, but in separate rooms.

Both grafts have the same 3 year graft survival rates (80-90%).

Preoperative Management:

1- Preoperative Patient Evaluation, Preparation and Premedication:

First correct **the recipient's medical condition** as the patient has chronic renal failure:

- Serum K^+: should be < 5.5 mEq/L.

• Coagulopathy should be corrected.

2- Immuno-Suppressive Therapy Protocol:

The use of immunosuppression for kidney transplantation is divided into 3 periods:

1- Induction Phase: It involves administration of medications that provide marked immune suppression before and during the first week of post-transplantation. Induction agents include thymoglobulin, OKT 3, daclizumab, basiliximab, or corticosteroids.

2- Maintenance Phase: It involves administration of agents continuously for 3-6 months to prevent acute rejection. These medications are also given to induce tolerance. Tolerance means unresponsiveness by the recipient to the kidney graft in absence of maintenance immunosuppression. Tolerance can decrease the use of long-term medications, reduce adverse effects, and improve the quality of life.

3- The third Phase: beyond 6 months when long-term immunosuppression is established. The regimen will be maintained for the rest of the life of the transplant recipient.

Immunosuppressive agents consist of:

1- Corticosteroids:

Preoperatively: methyl prednisolone (*Solu-medrol*) 250 mg i.v.

Postoperatively: methyl prednisolone (*Solu-medrol*) 250 mg i.v. twice/day for 2 days followed by 125 mg i.v. twice/day for another day then the steroid doses are decreased (tapering) over 6 months.

2- Cyclosporine or cyclosporin (*Neoral*):

It is started 7 days before transplantation of a living-donor kidney,
but 1 day after transplantation of a cadaveric kidney.

N.B.: Some centers avoid cyclosporine and replace it by **monoclonal antibodies** directed against specific subsets of T lymphocytes.

3- Azathioprine:

It is started 2 days before transplantation of a living-donor kidney,
but on the same day of transplantation of a cadaveric kidney.

N.B.: Some centers replace azathioprine by **Mycophenolate mofentil** (*Cellcept*) (1 g twice daily) started 1day before transplantation of both types of kidney grafts and stopped after 6 months for cadaveric kidney and after 3 months for living donor kidney transplants.

4- Tacrolimus (*Prograf*):

It is started 1 day after transplantation of both living donor and cadaveric kidneys.

Most immuno-suppressive therapies are maintained **for 6 months**.

Side effects of immunosuppressant agents such as nephrotoxicity, hepatotoxicity, hypertension ...etc, are discussed in the chapter of "Pharmacological Adjuncts to Anesthesia and Intensive Care".

Calcium channel blockers: are added to the immuno-suppressive protocol.

Value: It allows using relatively higher doses of cyclosporine without adversely affecting the renal functions as they oppose cyclosporine/tacrolimus-mediated renal vasoconstriction.

Agents: • Nifedipine is the most commonly used, given orally pre- and immediately postoperatively.
• Verapamil, diltiazem and nicardipine are not used because they can interfere with the P 450-mediated degradative metabolism of cyclosporine and tacrolimus resulting in an increase in their half lives.

N.B.: Verapamil 10 mg is given intra-arterially after arterial anastomosis in cadaveric kidney transplants.

3- Complete Aseptic Precautions against Infection:

It is essential due to the immunosuppressant effects e.g., use sterile disposable anesthetic circuit.

Intraoperative Management:

Aim:

A high normal systemic blood pressure is required in the presence of euvolemia to maintain adequate urine flow.

Choice of Anesthesia:

• Regional anesthesia (spinal or epidural): can be used with care for coagulopathy and hypotension.
• General anesthesia: is commonly used.

Monitoring:

Besides the standard monitors,

• **Central venous pressure** is essential for fluid balance to allow adequate hydration and avoid fluid overload.
• **Urine output** may indicate the adequacy of the graft.
• Serum electrolytes for K^+.

Intraoperative Complications:

1- The same anesthetic management for **patients with chronic renal failure.**

2- The graft Preparation and Anastomosis:

• The transplantation is carried out by placing **the donor kidney retro-peritoneally** in the iliac fossa and anastomosing the renal vessels to the iliac vessels and the ureters to the bladder. The right kidney is placed in the left groin and the vice versa.

• **In living-related grafts:** After removal of the kidney from the donor, it is flushed immediately with iced ringer lactate solution containing heparin and mannitol allowing ischemic time to be between 20-30 min.

• **In cadaveric grafts:** Before release of the arterial clamp and after completion of the anastomosis, an intra-arterial injection of **verapamil 10 mg is given by a direct push into the kidney.**

• **Furosemide 200 mg** is given for both grafts immediately after completing the anastomosis.

3- Problems of Release of the Vascular Clamp:

After completion of the arterial anastomosis, the vascular clamp is released resulting in:

- **Hyperkalemia** due to K^+ release from the preservative solutions or from the lower limbs (if external iliac vessels were clamped). This may cause sudden cardiac arrest.
- Transient **metabolic acidosis** due to reperfusion of ischemic legs.
- **Hypotension** due to the abrupt distribution of up to 300 mL blood to lower limbs and the release of vasodilating chemicals from previously ischemic tissues. It is treated by i.v. fluids.
- **Hypertension** may occur due to:
  - release of renin from the donor kidney.
  - release of catecholamines from the intact adrenal gland of the donor kidney; so, it should be excised.

4- After Transplantation, Adequacy of the Graft should be assessed:

• A **brisk urine output** usually occurs after arterial anastomosis which indicates **good graft function** (this diuresis may resemble non-oliguric renal failure).

• If an **oliguric phase** precedes the diuretic phase, this indicates **prolonged graft ischemic time or mechanical impingement of the graft, vessels, or ureters;** so, fluid therapy must be adjusted appropriately and mannitol 0.25-0.5 g/kg should be given to facilitate urine formation in the transplanted kidney (unlike the loop diuretic furosemide, mannitol does not depend on renal tubular concentrating mechanisms to produce diuresis).

• If **sudden increase in body temperature** after transplantation occurs and the graft becomes swollen and dark, this indicates **super-acute rejection** (the graft has to be removed).

5- Drug Clearance of the newly Transplanted Kidney:

A newly transplanted, but functioning kidney is able to clear neuromuscular-blocking drugs and the anticholinesterase drugs used for their reversal at the same rate as normal patients.

Fluid Therapy:

Amount:

• **Adequate** fluid volume should be given to optimize renal blood flow and improve early function of the transplanted kidney (to avoid postoperative renal failure) because patients tend to be hypovolemic.

• The cadaveric kidney requires higher plasma volume and higher blood pressure to initiate diuresis than the normal kidney. Therefore, keep the systolic blood pressure around 130-160 mm Hg and the central venous pressure around 10-15 cm H_2O.

• Anuric patients typically need 8 mL/kg/day to replace the insensible water loss (in adults, insensible water loss is 500-600 mL).

Type:

• **Half normal saline** is preferred to normal saline by some anesthesiologists to decrease the Na^+ load on the new kidney.

• K^+ containing solutions should be avoided:

• 5% albumin can be used.

• Blood transfusion is indicated in severe blood loss or when hematocrit is < 15%. **Packed washed red blood cells** (leukocyte-poor blood) are given to avoid rejection because introduction of leukocytic antigen can cause production of additional antibodies predisposing to rejection of a subsequently implanted kidney.

Postoperative Management:

Most patients are extubated postoperatively.

Postoperative anesthetic management of the recipient is nearly the same as that of **patients with renal impairment.**

Postoperative complications include:

1- **Graft failure (i.e., acute renal failure):** Acute tubular necrosis in the transplanted kidney may occur due to prolonged ischemia or cyclosporine toxicity. It is treated by hemodialysis.

2- **Rejections** are: **super-acute** (that usually occurs intraoperatively),
acute (hours to weeks), or
chronic (months to years): presented by fever, decreased urine output, increased serum creatinine, renal enlargement and tenderness similar to pyelonephritis or recurrent glomerulopathy. They can be differentiated by renal biopsy. It is treated by corticosteroids and anti-lymphocyte globulins.

3- Complications due to arterial connection; vascular spasm or occlusion (**renal artery occlusion**).

4- Complications due to venous connection; **hemorrhage and hematoma** resulting in vascular or ureteric obstruction.

5- Complications of lymphatics e.g., **lymphocele** because lymphatics are not connected during surgery.

6- Complications due to lumen connection; a leak such as a **ureteric leak (and urinary fistula)**.

7- **Infections** due to immunosuppression.

8- **Increased incidence of cancer** due to chronic immuno-suppression such as large-cell lymphoma.

Anesthesia for Renal Transplant Recipients undergoing Other Surgery

Anesthetic Problems

- Patients are often **elderly with co-existing** cardiovascular **disease**, diabetes mellitus, and hypertension (and receiving their corresponding medications with their side effects).
- Patients are receiving **immunosuppressant drugs with their side effects** such as systemic hypertension, lowered seizure threshold, anemia, thrombocytopenia…etc that should be considered during anesthetic management. They are discussed in the chapter of "Pharmacological Adjunct in Anesthesia & Intensive Care".
- **The function of the transplanted kidney should be assessed.**
  - **Serum creatinine concentrations** are likely to be **normal** in the presence of normally functioning renal transplant.
  - **The glomerular filtration rate and renal blood flow** are likely to be **lower** than those of healthy individuals, and the activity of **drugs excreted by the kidneys** may be **prolonged.**
  - **The presence of azotemia, proteinuria, and systemic hypertension** may indicate **chronic rejection** of the kidney transplant.
- **Drugs that are potentially nephrotoxic or dependent on renal clearance are avoided.**
- **Diuretics** are administered only with careful evaluation of the patient's intravascular fluid volume status.

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Web sites:

- http://www.auanet.org/guidance/
- http://www.kidney.org/news/newsroom/fsitem.cfm?id=30

ORTHOPEDICS

18

• General anesthetic problems. • Hip surgery. Fracture neck femur Total hip replacement (arthroplasty). Pelvic and acetabular trauma.	• Knee surgery. Knee arthroscopy. Total knee joint replacement.

General Anesthetic Problems and Considerations

1) Type of the Patient:

1. The patients are usually **elderly** with:
   - **coexisting diseases** such as cardiovascular, respiratory, diabetic…etc which need preoperative detection and management.
   - **arthritic diseases** such as osteoarthritis and rheumatoid arthritis. Rheumatoid arthritis needs special precautions because it is associated with systemic affection such as:
     - Pericardial effusion, myocarditis, coronary arteritis, conduction defects, vasculitis, and aortic regurgitation.
     - Pleural effusion and interstitial pulmonary fibrosis.
     - Anemia, eosinophilia, platelet dysfunction (due to aspirin therapy), and thrombocytopenia.
     - Adrenal insufficiency (due to corticosteroid therapy) and impaired immune system.
     - Atrophic and thin skin.
     - Joint affection especially tempro-mandibular and cervical vertebral joints.
     - Side effects of non-steroidal anti-inflammatory drugs, corticosteroids, immunosuppressive therapy.

   Rheumatoid arthritis is discussed in the chapter of "Skin & Musculoskeletal Diseases".
2. The patients may be poly-traumatized; so, **other associated injuries** may be present.

2) In Case of Polytrauma:

a- Primary Survey (and Resuscitation) Measures:

- Primary survey and resuscitation measures should be **started at once**. **Advanced Trauma Life Support (ATLS) guidelines** should be taken which include:
  - A: control of the airway with cervical spine control.
  - B: breathing and ventilation.
  - C: circulation with hemorrhage control.
  - D: disability/neurological status.
  - E: exposure (assessment or evaluation) of all injuries.
- **Management of the hemorrhagic shock** should be initiated as soon as possible such as oxygenation, cannulation, arterial blood gases, colloid, crystalloids, or blood transfusion.
- **The patient's response to fluid resuscitation** should be assessed as follows:

An initial volume load (2 liters of pre-warmed crystalloids) is given. The patient's response is as follows:

- **The responder:** This patient does not require more fluid than the initial crystalloid given.
- **The transient responder:** This patient may need typed and cross-matched blood, fresh frozen plasma, or platelets. A urinary catheter and a nasogastric tube should be inserted if there are no contraindications. If hypotension (systolic blood pressure < 90 mm Hg) occurs in transient response patient, urgent surgery for damage-control procedures should be done.
- **The non-responder:** They need life-saving surgical treatment and all patients must be kept warm. The lethal triad which indicates the damage-control surgery includes:
  - hypothermia (< 34°C).
  - coagulopathy (prothrombin time > 19 sec or platelet count < 90 000/μL).
  - acidosis (pH < 7.2 or lactate > 5 mmol/L).

b- Secondary Survey:

It does not begin until the primary survey has been completed. It is a **head-to-toe evaluation** which involves in-depth evaluation by full history and examination to detect:

- other traumas.
- other concomitant medical conditions, allergies, and last meal intake.
- full neurological assessment.

3) The size of the operation is very important to be known by the anesthesiologist to:

- provide adequate preparation of the patient as i.v. lines and blood units.
- expect blood loss.
- expect complications because prolonged surgery and anesthesia will inevitably cause a great cytokine release and there is a very great risk that by the end of the surgery or in the immediate postoperative period to have acute respiratory distress syndrome even if there is minor chest trauma.

To avoid this, surgery should be postponed until the lung injury has healed or settled.

4) Increased Blood Loss:

Blood conservative therapy is essential to decrease blood loss and decrease blood transfusion. Blood loss can occur during:

1. Preoperative Period: Especially in hip and femur fracture (see later). It should be replaced before anesthesia.

2. Intraoperative Period:

Factors increasing bleeding:

- Aspirin therapy for arthritic diseases.
- Surgical techniques and experience.
- Previous surgeries e.g., hip surgery.
- Presence of femoral neoplasm or Paget's disease.
- Hypercapnia and hypoxia.

Factors decreasing bleeding:

1- **Tourniquet** e.g., knee surgery.

2- **Controlled hypotensive anesthesia**.

3- **Epidural and spinal anesthesia**: There is less blood loss than general anesthesia in spite of maintaining similar mean arterial blood pressure; the reason for this is uncertain, but may include differences in the resulting vasodilatation of the venous and arterial vascular system. This causes redistribution of blood flow.

4- **High dose aprotinin**: Aprotinin is a protease inhibitor of fibrinolytic activity and of the intrinsic coagulation pathway. It decreases blood loss in some patients, but should be used only for high risk cases (e.g., coagulopathies) because it produces allergy.

5- Intraoperative **blood salvage** (cell savers) and preoperative **autologous blood donation** can be used.

3. Postoperative Period: Careful monitoring and replacement of blood loss is important.

5) Increased Incidence of deep venous thrombosis (DVT):

The incidence is increased because they are elderly patients, with prolonged immobilization or with circulatory occlusions. **Prophylactic measurements should be taken**. They are discussed in the chapter of "Respiratory Diseases".

6) Increased Incidence of Fat Embolism (and Fat Embolism Syndrome):

Fat embolism can occur with long bone fracture. Its clinical picture, diagnosis, and management are discussed in chapter of "Respiratory Disease".

7) Patient Position:

During orthopedic surgeries different positions may be needed such as:

- Supine position that is used for upper limb and lower limb (below hips) surgeries.
- Lateral position that is used for hip surgery (with the affected limb uppermost).
- Prone position that is used for spine surgery.

The precautions and side effects of these positions should be considered.

8) Complete Aseptic Conditions:

Complete aseptic conditions are necessary especially for arthroplasty (hip or knee replacement).

- The surgery may be done under a laminar flow hood with the anesthesiologist and equipment outside the boundary.
- Prophylactic antibiotics should be given and the anesthesiologist should check that.

9) Intraoperative Radiology:

- Wearing a lead apron (which doubles the distance from the source and decreases the dose 4 folds) and turning away at moments of exposure to decrease thyroid and lens damage are advised.
- Intraoperative fluoroscopy and arthroscopy may need darkness in the operating room.

10) Postoperative Analgesia:

It is mandatory because early mobilization is an important factor for decreasing morbidity, but excessive sedation should be avoided in elderly age.

Choice of Anesthesia

A) Regional Anesthesia: such as spinal or epidural anesthesia.

It is more preferred in association with light i.v. sedation.

Advantages:

1. Little effects on cardiovascular and respiratory system.
2. It decreases blood loss (see above).
3. It decreases the risk of aspiration.
4. It decreases the risk of DVT because:
   - It allows greater lower limb venous blood flow due to sympathectomy.
   - It decreases platelet activity.
   - It attenuates the postoperative increase in factor VIII and von Willebrand factor.
   - Local anesthesia has an anti-inflammatory action.
   - It attenuates the postoperative decrease in anti-thrombin III.
   - It changes stress hormone release.
5. It allows postoperative analgesia for rehabilitation.

B) General Anesthesia:

1) I.v. Agents only: by single dose.

It is used for short procedures as manipulation of a stiff joint or closed reduction.

2) Controlled Ventilation with Muscle Relaxants:

It is used for long and complex procedures especially with abnormal patient positions.

N.B.: Some combine regional block such as epidural anesthesia with light general anesthesia for hip surgeries to get the advantages of both.

Hip Surgery

I) Fracture Neck Femur

It is associated with high mortality rates 10% after initial hospitalization and 25% within 1 year of fracture.

Anesthetic Problems:

In addition to the general anesthetic problems as above (from 1 to 10):

11) Type of Patient:

Patients usually have severe pain on moving the limb; therefore,

- They may need good premedications (but in small doses due to old age).
- Anesthesia may be induced, while the patient is still on his/her bed (which is brought to the operating room).

12) Blood Loss:

Generally, the amounts of blood loss from hip fractures depend on the location of the fracture. Fractures are arranged in order from the least to the most bleeding fracture (figure 18-1).

Intra-capsular fractures (are with less bleeding because the capsule acts as a tourniquet).

- Subcapital.
- Transcervical.

Extra-capsular fractures (are associated with more bleeding)

- Base of neck.
- Intertrochanteric.
- Subtrochanteric.

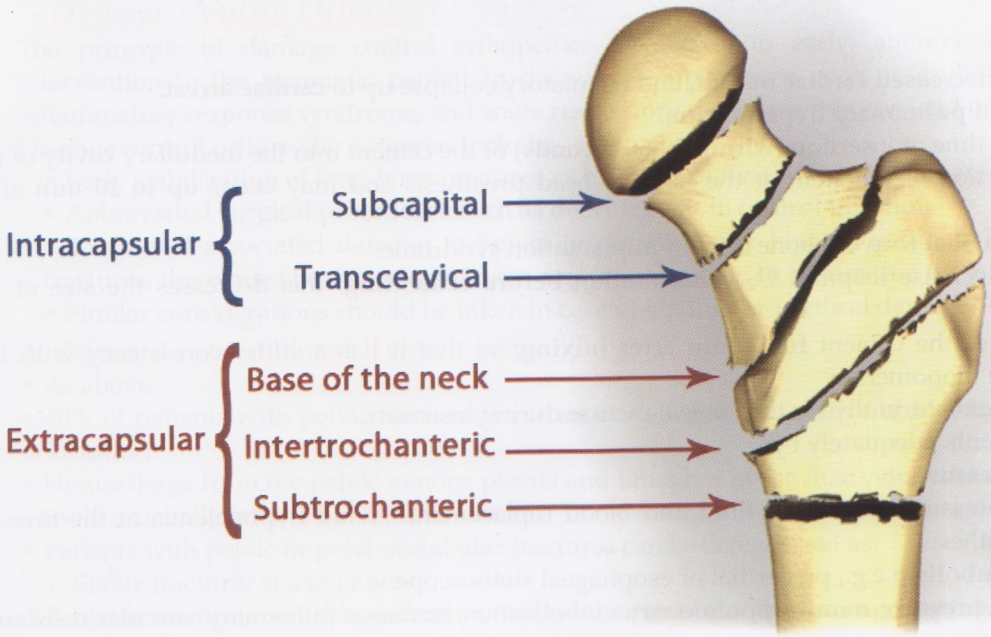


Figure 18-1: Fracture neck of femur

Choice of Anesthesia:

The same as above, in addition to:

- **Para-median approach** that is more suitable in elderly patients (in spinal or epidural) because:
  - It avoids the frequently calcified interspinous ligaments.
  - It can be performed without optimum flexion of the patient.
- **Hypobaric local anesthetics**: can be used as they allow easier positioning because the patient does not have to lie on the fractured hip.

II) Total Hip Replacement (Arthroplasty)

Anesthetic Problems:

In addition to the general anesthetic problems as above (from 1 to 10):

11) Paget's Disease of Bone:

It is usually present in candidates for total hip replacement. It causes hyperemia of the bone leading to **arterio-venous anastomosis**. This results in low peripheral resistance and **high cardiac output failure.**

12) Bone Cement Implantation Syndrome:

Cause:

Acrylic bone cement (poly-methylmethacrylate cement)

- It is used to fix the artificial joint component in place (Thompson prosthesis).
- It consists of 2 components, a liquid and a powder, both are mixed together before use. This reaction liberates heat i.e., exothermic reaction, and forms a doughy polymer, which expands and increases the intra-medullary pressure.
- Its use may cause bone cement implantation syndrome due to one of the following causes:

  1- A reaction to the heat generated when the cement is set. It may cause **air embolism.**

  2- Toxic or vasodilator effects (and tachycardia) of free liquid monomers absorbed into the circulation.

  3- Cement anaphylaxis.

  4- Autonomic effects secondary to the pressure rise within the femoral shaft.

  5- Embolism from the medullary cavity (air, polymer particles, or fat as 'the cement is a fat solvent' due to resultant intra-medullary hypertension **> 500 mm Hg**).

  6- Release of **tissue thromboplastin** may trigger platelet aggregation leading to micro-thrombus formation in the lung. This in turn causes:

- Cardiovascular instability due to circulation of vasoactive substances.
- Vasoconstriction of pulmonary vessels and bronchioles resulting in ventilation/perfusion mismatch and hypoxia.

Clinical Picture:

1- Hypotension, decreased cardiac output, and circulatory collapse up to **cardiac arrest.**

2- Hypoxemia and pulmonary hypertension.

They occur at the time of insertion (**within 30-60 seconds**) of the cement into the medullary cavity of the femur and impaction of the stem of the femoral head prosthesis and may occur **up to 10 min** after insertion.

Precautions: are essential to avoid bone cement implantation syndrome.

1- Stop N_2O and increase inspired O_2 concentration **before cementing**; this decreases the size of air emboli if they occur.

2- Delay insertion of the cement **for 2 min after mixing;** so that it has a stiffer consistency with the presence of less free monomers.

3- Observe the patients carefully for the clinical picture during insertion.

4- Monitor the patients adequately by:

- **Invasive blood pressure**.
- **Central venous pressure** for proper fluid and blood replacement. Avoid hypovolemia at the time of insertion of the prosthesis.
- Monitors for **air embolism** e.g., precordial or esophageal stethoscope.
- **Pulmonary artery pressure monitor**; pulmonary embolization increases pulmonary vascular resistance (PVR) which increases pulmonary artery pressure (PA) without change in pulmonary capillary wedge pressure (PCWP). It also decreases cardiac output (CO).

$$PVR = \frac{PA - PCWP}{CO} \times 80$$

5- Perform high pressure lavage of the femoral shaft to remove debris (potential micro-emboli).

6- Perform venting of the medullary cavity to decrease the pressure effect. This pressure is produced by the piston effect of impaction of the prosthesis's stem into the cement filled medullary cavity. This is best done before inserting the cement and the prosthesis by:

- drilling the bone cortex.
- passing a catheter down the shaft.

N.B.: Bilateral hip replacement can be safely done in one sitting assuming that no significant pulmonary embolization occurs after the 1st hip replacement. If pulmonary artery resistance increases > 200 dynes sec/cm^5 (which is the normal value) during the 1st hip replacement, the contra-lateral surgery should be postponed.

N.B.: There are 2 types of femoral head replacement prosthesis:

- Thompson prosthesis needs cement for fixation.
- Moore prosthesis does not need cement for fixation, thus avoiding the side effects of the cement.

III) Pelvic and Acetabular Trauma

There are significant differences between pelvic and acetabular fractures:

	Pelvic Fractures	Acetabular Fractures
Hemorrhage	Major depending on the fracture pattern	Minimal
Hemodynamic instability	Present	Usually absent
Late post-traumatic arthritis	Usually absent	Usually present especially if there is major primary articular surface loss or if fracture remains poorly reduced after treatment due to callus formation that hinders the possibility of complete surgical reduction of the fracture.

In addition to the general anesthetic problems and considerations as above (form 1 to 10), the following anesthetic management (pre-, intra-, and postoperative) should be considered.

Preoperative Management

1- Damage Control Orthopedic Surgery:

The principle of damage control orthopedics means to do early, abbreviated, and least invasive intervention to the traumatic patient to decrease complications such as multi-organ failure, systemic inflammatory response syndrome, and acute respiratory distress syndrome, and decrease mortality rates.

Damage control orthopedic surgeries include:

- Early stabilization of long-bone fractures as by external fixation to control hemorrhage.
- Abbreviated surgical procedures such as debridement to control infection.
- In case of associated damage to bowel (especially large bowel), particularly in the case of pelvic fractures, there must be diversion of feces e.g., by colostomy to ensure that the fracture site is kept clean.
- Similar considerations should be taken in case of bladder or urethral damage.

2- Primary Survey (and Resuscitation) Measures:

- As above.
- 40% of patients with pelvic fractures have an intra-abdominal source of bleeding (liver, spleen, bowel, or bladder).
- Hemorrhage from the pelvic venous plexus and branches of the iliac veins is major and that from major vessels is usually fatal.
- Patients with pelvic or pelvi-acetabular fractures can be categorized as:
  1- Stable fracture/stable patient.
  2- Stable fracture/unstable patient (consider other source of hemorrhage e.g., abdomen).
  3- Unstable fracture/stable patient (i.e., responder).
  4- Unstable fracture/unstable patient (i.e., transient or non-responder)

Steps to control and prevent further pelvic bleeding associated with pelvic fractures

1- Pelvic binding such as:
  - avoiding unnecessary movement of the patient.
  - using pelvic binders or if not available, wrapping a sheet around the pelvis and pulling this tight to close the open pelvic fracture. This may tamponade the blood loss.
  - Wrapping the legs together (internal rotation and adduction of the lower limb). This will partially reduce the fracture.

2- External fixation devices can be used as emergency tools.

3- Packing by emergency laparotomy in severe bleeding cases.

4- Internal fixation by urgent open reduction and internal fixation.

5- Embolization either arterial or venous, under x-ray control, performed in radiology department for modest bleeding (e.g., a patient requiring 2-3 units of blood every 24 hours). It is not available in all centers.

N.B.: Potential spinal fracture precautions are maintained until the spine is clinically and radiographically cleared.

3- Secondary Survey:

As above.

4- Definitive Care:

- After the primary, secondary survey, damage control surgery is indicated (it can be done before secondary survey to be completed) as before.
- The patient may be transferred to a more specialized orthopedic center.

Indications for Urgent Pelvic Surgery (day 0):

1- Acute pelvic bleeding control in non-responders to fluid/blood resuscitation and wrapping of legs/pelvis: They need external fixation, packing by laparotomy, open reduction and internal fixation, or wiring.

2- Open fractures with/without bowel/bladder violation: They need:
  - Antibiotics, tetanus, debridement/lavage, povidone-iodine dressing.
  - If bowel or bladder violation, they need also urinary and fecal diversion (de-functioning colostomy).
  - If the wound is not clean, external fixation and traction are needed.
  - If the wound is clean, definitive surgery is done.

Definitive surgery is done as soon as possible only when the patient is hemodynamically stable.

3- Vascular or neurological compromise.

4- Polytrauma needs damage control surgery.

Indications of Urgent Acetabular Reconstruction:

1- Open fractures.
2- Worsening neurological status.
3- Vascular compromise.
4- Irreducible fracture dislocation.
5- As a part of an acute pelvic fixation.
6- Acetabular fractures with urological injury.
7- Hip instability (recurrent dislocation) despite traction.
8- Acetabular fracture with ipsilateral femoral fracture.

Intraoperative Management:

Operative-size Classifications

Size of Operation	Examples	Likely Blood Loss	Blood Cross Match	Requirements
Small (operative time < 2 hours)	• Posterior wall fracture. • Isolated symphysis pubis diastasis. • Isolated iliac crest fracture. • External fixators.	< 1 liter	4 units	• Two large bore i.v. cannulas. • Urinary catheter.
Medium (operative time 2-4 hours)	• Anterior acetabular fracture fixation. • Anterior pelvic fixation.	1-2 liters	6 units	As above + • cell saver • ± Central venous catheter. • ± Arterial line. • ± Intensive care unit bed.
Large (operative time 4-6 hours)	• Open anterior and posterior pelvic surgery. • Anterior and posterior acetabular fracture.	2-5 liters	8 units	As medium + • Central venous catheter. • Arterial line. • Intensive care unit bed.

Any of the following conditions will put the patient at a higher group. If the patient is already in the large group, and a higher group is needed, a suffix of "+" may be added.

- Combined acetabular and pelvic surgery.
- If the patient has serious concomitant injuries to other parts of the body especially cardiovascular and respiratory systems.
- If injuries are more than two weeks old.
- If other procedures are performed at the same time.

Choice of Anesthesia

a- Regional Anesthesia:

Disadvantages: It is not appropriate in fractured pelvis due to the following:

- The patient is unable to sit up or turn on his/her side or curl up sufficiently to perform epidural anesthesia due to pain.
- Many patients have nerve damage from the original accident or postoperatively from the surgery itself. This necessitates assessing the neurological state of the limbs after surgery which cannot be achieved in the presence of a regional block.

b- General Anesthesia:

Most patients are young and fit (most being victims of motor vehicle accidents); therefore, the general considerations are taken.

Postoperative Management:

Factors that increase mortality:

1- Age; the adult patients are affected worse than the pediatric patients.
2- Hypotension on arrival at the resuscitation room (transient or non-responders).
3- Pelvic instability (as there is a greater degree of vascular instability).
4- Extent of wound (as large soft-tissue trauma or degloving).
5- Presence of rectal injury.

Complications Associated with Pelvic or Acetabular Fractures:

	Immediate	Early	Late
a) Pelvic Fracture	• Hemorrhage • Systemic inflammatory response syndrome • Urethral or bladder disruption • Rectal perforation • Vaginal wall laceration	• Transfusion-related acute lung injury • Adult respiratory distress syndrome (ARDS) • Multiple organ dysfunction syndrome (MODS) • Coagulopathy up to disseminated intravascular coagulopathy (DIC)	• Chronic pelvic pain • Erectile dysfunction • Urethral stricture
b) Acetabular Fracture	• Hip dislocation	• Hip dislocation	• Post-traumatic osteoarthritis • Leg length discrepancy
c) Both Pelvic and Acetabular Fractures	• Emboli (thrombus, fat, or air) • Sciatic, sacral plexus, femoral, and obturator nerve injury	• Nerve palsies • Septicemia, wound infection. • Hematoma	• Trendelenburg gait • Psychosocial problems as post-traumatic stress disorder • Growth arrest in pediatric patients

Knee Surgery

I) Knee Arthroscopy

Anesthetic Problems:

In addition to the general anesthetic problems as above (from 1 to 10):

11) Tourniquet: see below.

12) Outpatient Anesthesia:

Early postoperative ambulation is required with good pain relief. This is achieved by:

- **Intra-articular bupivacaine** 20-30 mL of 0.25% with 1: 200 000 epinephrine is usually used with/without morphine 3-5 mg. This causes prolonged analgesia for several hours. The exact mechanism is controversial. It may be due to the presence of peripheral opioid receptors in the joints.
- **Block of the femoral and sciatic nerves** (with or without obturator nerve block) are needed. Three-in-one block of Winnie (unreliable) or psoas compartment block (reliable) can block the femoral, obturator, and lateral femoral cutaneous nerves of the thigh together by one injection.

Heavy opioids should be avoided.

II) Total Knee Joint Replacement

Anesthetic Problems:

In addition to the general anesthetic problems as above (from 1 to 10):

11) Bone Cement Implantation Syndrome:

It is discussed above, but cement is very rarely used in knee joint replacement.

12) Tourniquet:

Aim:

Tourniquet creates a bloodless field to facilitate surgery.

Technique:

The same principles are used for upper limb tourniquet.

- Pneumatic type is used; it should be **padded especially in thin patients**.
- The limb should be **elevated for about 1 min**, then elastic exsanguination by **Esmarch bandage** is used prior to the tourniquet, but **not in** cases of **fractures, sepsis, sickle cell anemia, and neoplasm.**
- The **best sites** are the **midpoint of the thigh** (for lower limb) and the **upper arm** (for upper limb) as they have the greatest muscle bulk, thus avoiding nerve injury.

• Pressure used **in upper limb** is 50 mm Hg above systolic blood pressure **(up to 300 mm Hg)** for **1 hour**, while pressure used **in lower limb** is 100 mm Hg above systolic blood pressure **(up to 500 mm Hg)** for **1.5-2 hours**.

• Reperfusion after 1-2 hours of inflation followed by reinflation is not universally recommended as some believe it supplies more substrates for free radical production without prolonging safe inflation time.

Disadvantages:

1- Tourniquet of **both lower limbs** increases **central venous pressure and arterial blood pressure** which may cause serious effects in patients with **compromised cardiac function** especially in infants and elderly patients; therefore, bilateral lower limb tourniquet should be avoided.

2- **Prolonged or incorrect application of the tourniquet** may produce:

- **soft tissue** damage with bruising,
- **nerve** damage,
- **vascular** damage with increasing incidence of **DVT** in lower limbs, and
- transient **muscular dysfunction** and even **rhabdomyolysis**,

3- **Tourniquet pain:** severe aching and burning pain which may increase blood pressure about 1/2-1 hour after cuff inflation depending on many factors such as:

- Anesthetic techniques; i.v. regional > epidural > spinal > general anesthesia.
- The intensity and level of block.
- The choice of local anesthetics: spinal anesthesia with hyperbaric tetracaine > isobaric bupivacaine.

4- Tourniquet application is associated with **increases in body temperature in pediatric patients** undergoing leg surgery.

5- **On release of the tourniquet**, the following can occur:

- **Hypotension and tachycardia** due to shift of the blood to the periphery or **reactive hyperemia** which causes **hemorrhage** especially with improper hemostasis.
- **Hyperkalemia** due to release of potassium from the ischemic tissues.
- **Metabolic acidosis** due to release of acids from the ischemic tissues resulting in increased $PaCO_2$.

Release of the tourniquet rarely causes clinical pictures except if bilateral lower limb tourniquets are used.

Contraindications:

1- **Peripheral vascular disease** as calcific arterial disease.

2- **Sickle cell disease or trait** is controversial, but it can be safely used in them after particular attention to maintain oxygenation, normo- or hypocarbia, hydration, and normothermia with keeping tourniquet time as short as possible.

N.B.: If non-depolarizing muscle relaxants are used in a patient with a tourniquet, avoid drugs such as atracurium which degrade spontaneously because once the preliminary dose has worn off, a further bolus (although effectively paralyzing the rest of the patient) will have no effect on the isolated limb which will continue to move throughout the procedure, embarrassing the surgeon and anesthetist alike. Therefore, use drugs which need liver or kidney clearance. It should be injected before the tourniquet application.

Spine Surgery

It is discussed in the chapter of "Central Nervous Diseases".

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OTORHINOLARYNGOLOGY 19

• Tonsillectomy/adenoidectomy. • Postoperative bleeding tonsil. • Endoscopic surgery of the larynx. • Laser surgery.	• Foreign body aspiration. • Head and neck cancer surgery. • Nasal and sinus surgery. • Ear surgery.

Airway safety is the most important consideration during otorhinolaryngological and head and neck surgeries because of the following reasons:

- The surgeon and anesthesiologist share the airway.
- The access for the anesthesiologist is limited by drapes and instruments.
- The problems of the underlying pathology and bleeding into the airway may endanger the airway.
- Anesthetic circuit disconnections are a constant threat during surgery.

Tonsillectomy/Adenoidectomy

Anesthetic Problems:

Anesthetic problems are summarized in the following points:

1- The type of patients: Patients are usually pediatrics with upper respiratory tract infection or obstructive sleep apnea syndrome.
2- Day case anesthesia.
3- Airway management.
4- Transmission of infections by surgical and anesthetic equipment.
5- Blood loss especially in young age.
6-- Postoperative tonsil position.
7- Risks of postoperative bleeding tonsils.

Preoperative Management:

- Patients are usually **young and healthy**, but may have one of the following conditions:
  - **Acute upper respiratory tract infection** (URTI): **Surgery should be postponed for 2 weeks** even after recovery because URTI causes hyperactive airway reflexes.
  - **Obstructive sleep apnea syndrome:** due to the effect of the **hypertrophied tonsils**. This causes a combination of prolonged partial upper airway obstruction and intermittent complete obstruction.

  Obstructive sleep apnea syndrome is presented by the following:
  In mild cases, habitual snoring is the most common symptom.
  In severe cases (1%), chronic hypoventilation occurs resulting in hypoxia and hypercarbia. This leads to:
  - Neuro-developmental problems such as excessive daytime somnolence, behavioral disturbances, school failure, recurrent enuresis, developmental delay and even failure to thrive.
  - Pulmonary hypertension and congestive heart failure which may cause death.

Therefore, preoperative evaluation for obstructive sleep apnea and preoperative management of its complications are needed.

- Precautions for **day-case anesthesia** if used should be taken. It is discussed later in the chapter of "Ambulatory Anesthesia & Sedation".

Premedications:

1. Sedatives: e.g., midazolam 0.5 mg/kg (to a maximum of 15 mg) oral syrup.
They are usually needed as patients are young children. They should be avoided in obstructive sleep apnea syndrome.
2. Anticholinergics: e.g., atropine 0.02 mg/kg (to a maximum of 0.6 mg) oral syrup.
They are usually needed to decrease salivation. They are better avoided in hot weather.
3. Topical local anesthetic cream such as EMLA cream may be applied on the hand 1 hour before i.v. cannulation (mark sites of veins).

Intraoperative Management:

Induction: It is either by:

1- I.v. agents (if i.v. cannula was inserted) followed by suxamethonium (premedication with atropine is essential).

or 2- Inhalation agents (sevoflurane) then i.v. cannula is inserted and intubation is performed.

Large tonsil may lead to respiratory obstruction which makes it difficult to maintain the airway. In case of obstructive sleep apnea, negative pressure pulmonary edema may occur.

Intubation:

- **Oral intubation** is the most common by:
  - a reinforced endotracheal tube to decrease the risk of kinking by the self-retaining mouth gag (Boyle-Davis gag).

or - a preformed RAE tube to direct the breathing circuit away from the field of surgery.

In adults, nasal intubation is preferred by some surgeons, but it may carry the risk of **bleeding** from adenoid trauma or even **implantation** of parts of adenoid in the trachea.

- **Laryngeal mask airway (LMA)** is recently used, usually the reinforced flexible type, for many types of otorhinolaryngological surgeries such as tonsillectomy. LMA offers relative good protection against aspiration of blood or surgical materials.

Advantages of LMA over endotracheal tubes: LMA avoids many of the problems associated with tracheal intubation such as bronchospasm or stress response which may increase congestion and bleeding.

Disadvantages of LMA:

- Surgical access is restricted.
- It is more prone to displacement during surgery, with potentially catastrophic results.

Transmission of infections:

Infections such as **variant Creutzfeldt-Jakob disease or bovine spongiform encephalopathy** can be transmitted, although rare, during adenotonsillectomy surgeries. Organisms or prions may accumulate in lymphoid tissue such as the tonsils and adenoids which are not reliably destroyed during standard methods of surgical sterilization. Inter-patient transmission of prions can occur via theater equipment contaminated during tonsillectomy/adenoidectomy.

In January 2001, the UK Department of Health issued guidelines that all relevant **surgical and anesthetic equipment used for tonsillectomy/adenoidectomy should be disposable**, including all airway equipment such as laryngoscope blades and laryngeal mask airways. In the case of expensive equipment, e.g., non-disposable laryngoscopes, the metal blade should be covered by a transparent sheath.

These guidelines (regarding disposable instruments) should be applied also for surgical instruments.

Blood loss:

It is usually mild intraoperatively. In children **weighting < 15 kg** (i.e., 3-4 years old), blood loss is considered large; therefore, **loss** of **100 mL blood** in them may **need blood transfusion.**

Extubation:

- **Awake extubation** in the lateral position with slight head down **(tonsil position)** is usually done.
- **Deep extubation** can be used, by a **senior staff**, to decrease coughing and laryngeal spasm and lessen the risk of bleeding especially in **a child with hyperactive airway disease** such as asthma, but the risk of aspiration may increase.
- **Suction:**
  - Suction should be done after careful **suction under direct vision** and ensuring that the pharynx is free from blood. Blind pharyngeal suction with a rigid sucker may cause bleeding from the tonsillar bed and should be avoided.
  - **Accumulation of blood behind the soft palate in the nasopharynx** should be avoided. This area is not readily visible and blood pooling here can be aspirated following extubation, with fatal results **"Coroner's clot"**. This area is best cleared either by using a soft suction catheter via the nose or by rotating a Yankauer sucker so that its angled tip is placed behind the uvula.

Postoperative Management:

1- The patient should be positioned left lateral/head down with the head turned to one side (**tonsil position**) to allow drainage of any residual oozing out of the mouth and to allow early detection of postoperative bleeding tonsils (figure 19-1).

2- **Postoperative analgesia** e.g., **rectal paracetamol** should be given at the end of surgery after obtaining consent from the parents. Use of **non-steroidal anti-inflammatory drugs (NSAIDs)** probably increases bleeding slightly (antiplatelet effects), but the clinical importance is doubtful. **Local anesthetic infiltration** of the tonsillar bed has been used by some.
3- In obstructive sleep apnea syndrome, intensive care admission is needed for close observation.
4- Postoperative bleeding tonsil can occur.

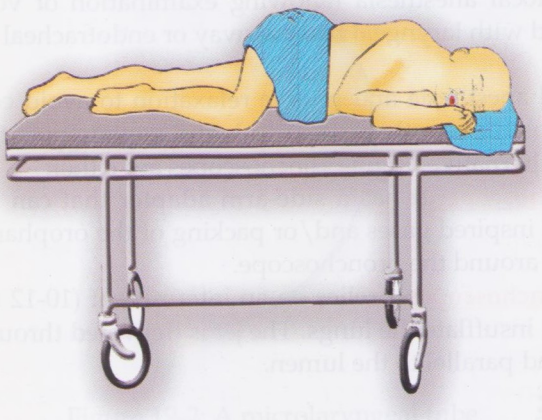


Figure 19-1: Tonsil recovery position

Postoperative Bleeding Tonsil

Anesthetic Problems:

1- Shocked patients.
2- Full stomach.
3- Blocked nose by the blood.
4- Postoperative laryngeal edema (due to intubation).

Preoperative Management:

• The patient is usually **hypovolemic and shocked,** with orthostatic hypotension, tachycardia, pallor, sweating, restlessness, up to altered state of consciousness. **Preoperative resuscitation** is very important by crystalloids or blood; otherwise, severe circulatory collapse may occur with induction.
• The patient has a **stomach full of blood** which increases the risk of aspiration. **Preoperative evacuation** of the stomach by a large-bore **naso-gastric tube** is important.
• Preoperative hemoglobin, hematocrit (early hematocrit usually falls due to i.v. fluids given), cross-matching blood and coagulation study are done.

Intraoperative Management:

• The patient is placed head down in a lateral position and the suction apparatus should be positioned within grasp before induction.
• Good preoxygenation is essential.
• Induction is performed by:
  a- **Rapid sequence crash induction** with **cricoid pressure** by using small dose thiopentone 3-4 mg/kg or etomidate or ketamine if there is any doubt about proper preoperative resuscitation where intubation is performed by succinylcholine 1-2 mg/kg or rocuronium (of choice).
  b- **Deep inhalational induction** may be used to facilitate intubation.
• **Cuffed oral** endotracheal tube (due to presence of blood in the nose) is used, but uncuffed tubes are used in children < 5-6 years old.
• Before awakening, **re-evacuate the stomach by a large bore naso-gastric tube** with care so as not to traumatize the adenoidectomy or tonsillectomy beds.
• **Awake extubation** is used in the lateral position.

Postoperative Management:

Laryngeal edema may occur due to re-intubation; therefore, dexamethasone i.v. and humidified O_2 should be administered.

Endoscopic Surgery of the Larynx (and Trachea)

Endoscopy includes laryngoscopy (diagnostic or operative), micro-laryngoscopy (laryngoscopy aided by an operating microscope), esophagoscopy, and bronchoscopy.

Types of Bronchoscopes (Currently in Use)

a- Flexible Fiberoptic Bronchoscope:

It can be used either **in awake sedated patients** (0.5 mg increments of midazolam and/or 10 µg of remifentanil boluses) under local anesthesia (allowing examination of vocal cords movements), or in patients generally anesthetized with laryngeal mask airway or endotracheal tube.

b- Rigid Bronchoscope:

It usually necessitates general anesthesia and muscle relaxation to avoid coughing or movement, which can cause tracheal trauma. Volatile anesthetics can leak and contaminate the operating room; therefore, total i.v. anesthesia is a valid alternative. Rigid bronchoscopes are either:

- **Rigid Ventilating Bronchoscope:** It has a side-arm adapter that can be attached to the anesthesia machine. High flow rates of inspired gases and/or packing of the oropharynx are needed because there is usually a variable air leak around the bronchoscope.
- **Rigid Venturi-Effect Bronchoscope:** It relies on an intermittent (10-12 times/minutes) high-pressure oxygen jet to entrain air and insufflate the lungs. The jet is delivered through a reducing valve into a 16- or 18-gauge needle inside and parallel to the lumen.

Anesthetic Problems:

1- Patients with upper airway problems.
2- An outpatient (ambulatory) procedure.
3- Deep general anesthesia and profound muscle relaxation.
4- Patient's head position.
5- Oxygenation and ventilation.
6- Cardiovascular instability.
7- Complications of the bronchoscope especially the rigid type.
8- Postoperative laryngeal spasm or edema.
9- Laser precautions.

Preoperative Management:

- Careful preoperative **assessment of potential airway problems** e.g., foreign body aspiration, tracheal stenosis, or obstructing tumors is essential by history, examination and **investigations such as CT scan, magnetic resonant imaging (MRI), or flow volume loops.**
- If the patient is suspected to have difficult intubation, 1st secure the airway before induction of anesthesia e.g., by fiberoptic bronchoscope, awake intubation or tracheostomy under local anesthesia.
- **All equipment** for **difficult intubation** should be available preoperatively.

Premedication:

- Sedatives are avoided if any degree of airway obstruction is suspected.
- Anticholinergics are used to decrease secretions and avoid bradycardia.

Intraoperative Management:

Laryngeal endoscopy is considered as **an outpatient procedure;** so, its precautions should be considered.

1. Deep General Anesthesia with Profound Muscle Relaxation:

Deep general anesthesia with profound muscle relaxation is usually indicated by **using a short acting non-depolarizing muscle relaxant** such as **mivacurium** or vecuronium (as it is usually a short procedure; about 5-10 minutes) **or by using succinylcholine infusion** to provide masseter relaxation for introduction of the suspension laryngoscope, but prolonged succinylcholine administration may cause phase II block.
In children, spontaneous ventilation without muscle relaxant may be used.

2. Patient's Head Position:

The patient's head should rest **on one pillow** with the neck slightly flexed and the head extended on the neck (i.e., sniffing position). A **gauze swab** is placed on the patient's upper teeth or gum **for protection.**
After the bronchoscope enters the trachea, the head of the table is lowered or the **pillow is removed carefully** so that the whole trachea comes into view.
To pass the bronchoscope into one of the main bronchi, the head is rotated to the opposite side to bring the bronchus into line with the mouth.

3. Oxygenation and Ventilation:

Oxygenation and ventilation are done by using 100% oxygen with one of the following techniques:

1) Coplan's Micro-Laryngeal Tracheal Tube or Mallinckrodt Critical Care Tube:

It is the most commonly used and can be used orally or nasally. It is **4, 5, or 6 mm** I.D., but **with the same adult length** (31 cm) and with a large high volume low-pressure cuff (filled with 10 mL) and is stiffer (less prone to compression) (figure 19-2).



Figure 19-2: A microlaryngeal tube

Advantages:

- Its small size will not impede the surgeon's view.
- Its cuff will prevent aspiration of blood or debris.
- It allows introduction of inhalational agents.
- It allows monitoring of $ETCO_2$.

2) Conventional Endotracheal Tube of Small Size:

Use one size smaller in children, but use size 4, 5 or 6 mm I.D. in adults.

Disadvantages: • It is **too short for the adult trachea**.
• It has a low volume cuff that will exert high pressure against the trachea.

3) Pollard's Tracheal Tube:

It is formed from latex reinforced with a nylon spiral. Its proximal end size is 10 mm I.D. and its distal end size is 5-7 mm I.D.

In 1, 2, and 3:

- Induction: Thiopentone and suxamethonium or short acting nondepolarizing muscle relaxant
  ± Spraying the vocal cord with 3 mL lidocaine 4% or painting with cocaine 3% to assist smooth anesthesia and decrease the risk of post-extubation laryngospasm.
- Maintenance: O_2 and N_2O, volatile agents, and controlled ventilation.

4) Intermittent Apnea Technique:

The ventilation and anesthesia are maintained with O_2 and a potent volatile agent (with a short acting muscle relaxant) by a facemask or an endotracheal tube for periods which alternate with periods of apnea during which the surgery is performed (usually 2-3 min). The oxygenation can be maintained by apneic technique via a small catheter alongside the bronchoscope. Apneic oxygenation is discussed in more details in the chapter of "Thoracic Surgery".

Pulse oximeter is essential. There is a risk of hypoventilation and aspiration.

5) Insufflation of High Flow of O_2 via a small catheter placed in the trachea.

6) Ventilation via a Side Arm of a Ventilating Bronchoscope:

Conventional spontaneous ventilation can be maintained through the side arm of a ventilating bronchoscope, which is connected to the breathing circuit. During suction or biopsy via this side arm, ventilation must be interrupted.

In both 5 and 6:

Anesthesia is maintained usually with **total intravenous anesthesia (TIVA)** while patients breathe **spontaneously**.

7) Manual Trans-Laryngeal Jet Ventilation:

It is a device that applies the oxygen under pressure. The jet injector such as **Sanders jet injector** (introduced in 1967), **or Enk oxygen flow modulator** is connected to a catheter which is applied trans-laryngeally (i.e., from the mouth, via the glottis, to inside the trachea as usual intubation).

It can be connected to a side port of the laryngoscope during laryngeal or tracheal surgery by the laryngoscope (figure 19-3).
Technique, complications, and contraindications are discussed in details in the chapter of "Airway Management".



Figure 19-3: Two different shapes of manual jet ventilation (left) and different sized-needles for jet ventilation (right)

8) High-Frequency Positive Pressure Ventilation:
Positive pressure ventilation is maintained at rates of 100-300 breaths/min. This technique eliminates air entrainment (i.e., no Venturi effect) and allows ventilation with an undiluted anesthetic gas mixture.
9) High-Frequency Jet Technique:
It is a variation of manual jet ventilation. It utilizes a small cannula (16-18 gauge) or tube placed in the trachea or in the proximal end of the bronchoscope through which gas is injected at **80-300 times per minute** at high pressure; therefore, a Venturi effect is created proximally, which entrains an air-O_2 mixture down the trachea. There is a risk of barotrauma and anesthetic gas dilution.

Capnography will tend to greatly underestimate the $PaCO_2$ during jet ventilation due to constant and sizable dilution of alveolar gases.
Carden tube is used during jet ventilation because it is made of malleable copper with a Luer connector at its proximal end that is attached to jet ventilation.
In 7, 8, and 9:
Anesthesia is maintained usually with **total intravenous anesthesia (TIVA)** while controlled ventilation is used.

4. Cardiovascular Stability:

Arterial blood pressure and heart rate fluctuate markedly during laryngoscopy and may need invasive arterial blood pressure monitoring because:

- Many patients are heavy smokers or alcohol drinkers which predisposes them to cardiovascular disease.
- The procedure resembles a series of stress-filled laryngoscopies and intubations separated by varying periods of minimal surgical stimulation.

Stable cardiovascular system should be maintained by:

- Supplementation with short acting anesthetics e.g., propofol or sympathetic antagonist e.g., esmolol (during periods of stimulation).
- Regional laryngeal nerve block.
  Glosso-pharyngeal nerve (at the anterior tonsillar pillar).
  Superior laryngeal nerve (near the hyoid bone).
- Topical anesthesia of the larynx with spraying 3 mL lidocaine 4%.

5. Complications of Bronchoscopy (Especially the Rigid Type):

1. **Trauma**:
   - Injury to teeth, lips, tongue, or oropharynx.
   - Injury to the **larynx, or trachea** resulting in postoperative laryngospasm and edema.
   - **Perforation of the airway** resulting in mediastinal or subcutaneous emphysema.
   - **Pleural perforation** resulting in pneumothorax.
   - **Pulmonary barotrauma** with venturi jet ventilation.
2. **Hypoventilation** causing hypoxemia, hypercarbia, and acidosis.
3. **Bradycardia and arrhythmias.**

6. Laser Precautions:

They are discussed below.

Postoperative Management:

Postoperative care includes:

- **Clearing of the airway** from secretions, blood, and debris.
- Keeping the patient during and after extubation in the **left lateral** head down position until becoming fully awake.
- Giving **humidified O_2**.
- **Close monitoring** for laryngospasm and edema is mandatory.

Laser Surgery

The word "Laser" is an acronym for **L**ight **A**mplification by **S**timulated **E**mission of **R**adiation.

Laser light differs from ordinary light in being:

- **monochromatic:** laser (and all photons) possesses one wave length.
- **coherent:** laser (and all photons) oscillates in the same phase.
- **collimated:** laser (and all photons) exists as a narrow parallel beam.

Advantages: It is used to strip polyps or tumors from the vocal cords.
It allows excellent surgical precision and preservation of normal tissues.
It allows good hemostasis.
It allows rapid healing and minimal scar formation.
It allows minimal postoperative edema and pain.

Physical Principles, Types, Features of Laser, and Effects of Laser on Tissues are discussed in the chapter of "Basic Physics for Anesthesia & Intensive Care".

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Hazards of Laser:

For the Patient:

1. **Airway fire:** It is the most dangerous during airway surgical procedures. Three components should be present for occurrence of a fire; they are called tripod of fire.
   - A flammable material or fuel (endotracheal tubes or tissue itself).
   - A source of ignition (laser beam).
   - A gas to support combustion (oxygen or nitrous oxide).

To prevent any fire from occurring, one of the limbs of the tripod should be removed.

2. **Injury** to normal tissues **adjacent to** the operative field e.g., tracheo-bronchial tree, perforation of major pulmonary blood vessels, teeth...etc.
3. **Hypoxemia** from inadequate ventilation, distal collection of secretions, blood, or debris, or smoke is a major cause of morbidity and mortality.

For Operating Room Personnel:

Toxic vapor and fumes (laser plume) from tissue vaporization leading to:

- Detrimental effects on pulmonary airway resistance, gas exchange and muco-ciliary function.
- Possible **infection** to operating room personnel as viable bacteria have been shown to be present in the laser plume (still not certain for viral particles as human immunodeficiency virus "HIV", papilloma-virus and hepatitis).

For Both:

1. **Eye damage:** CO_2 laser causes corneal opacities, whereas Nd: YAG laser causes retinal damage.
2. **Skin burns**: It varies from erythema to blisters or charring.
3. **Electrocution:** High voltage laser equipment may cause electric shock.

Protective Safety Measures:

1. Precautions Avoiding Airway Fire:

1) Avoiding Usage of Endotracheal Tubes:

Techniques that do not involve intubation are preferred such as intermittent apnea or jet ventilation techniques.

2) Laser Resistant Endotracheal Tubes:

They are used if intubation is mandatory. Laser resistant tubes are either originally designed for laser protection or they are ordinary tubes that are wrapped by a protective tape.

a. **Laser Resistant Tubes**: (each tube type is resistant to a specific type of laser) (figure 19-4).

- **Mallinckrodt Laser-Flex:** It is an air tight **stainless steel** spiral tube with **double polyvinylchloride (PVC) cuff**. It resists CO_2 laser (not Nd: YAG laser).
- **Rusch Laser-Tube:** It has a **soft rubber shaft** covered with a **corrugated silver foil** which is then covered by a **Merocel sponge covering tape (FDA-approved tape)**. The Merocel is moistened with saline which consumes laser energy if it is struck. It resists Nd: YAG laser.
- **Bivona Torre-cuff:** It is an **aluminum spiral tube covered with silicone** and has a unique self inflating foam sponge filled-cuff which remains expanded even after laser puncture.
- **Sheridan Laser-Trach**: It is a red rubber tube with a **copper foil tape** and is covered with polyester sleeve.
- **Xomed Laser Shield and Laser Shield II:**

They are **silicone-based** tubes wrapped with either **laser-reflective aluminum containing tape (Laser Shield) or reflective aluminum wrap with smooth fluoroplastic overwrap on the outside (Laser Shield II).**

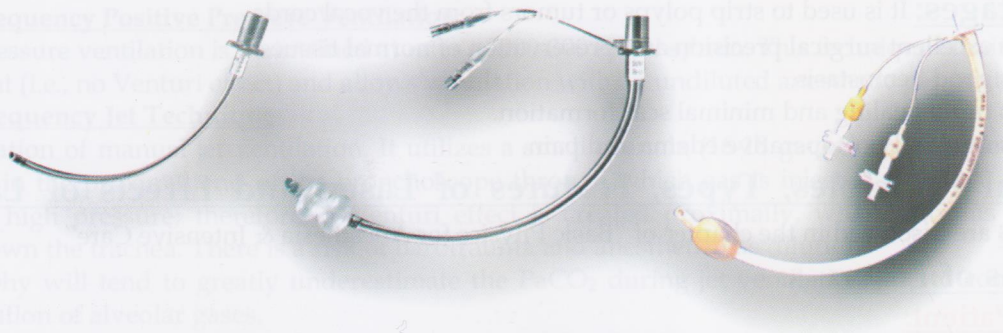


Figure 19-4: Laser endotracheal tubes

Advantages of laser resistant tubes:

- They are **kink resistant** tubes (for metal tubes).
- They are **combustion-resistant tubes,** but can still be ignited if enough laser energy is applied.
- They have double cuffs (a cuff within a cuff or a cuff above cuff); so, if the laser beam perforates one cuff, the other cuff will still seal the trachea.

Disadvantages:

- **They have a thick wall** (i.e., with a larger outer diameter for a given inner diameter than conventional endotracheal tubes) and are not available in pediatric sizes; therefore, they can not be used in small airways e.g., pediatric patients, tracheal stenosis, or obstructing lesions.
- They have decreased **flexibility**.
- They have more difficult cuff inflation and deflation properties.
- They can **transmit heat** (for metal tubes).
- They can **reflect laser** resulting in injury to the surrounding tissues.

b. **Polyvinylchloride (PVC) or Red Rubber Tubes:**

They are **wrapped by a metallic tape of aluminum or copper foil** in an overlapping spiral manner for several centimeters above the cuff. Nowadays, this practice is not accepted and is considered dangerous and should be avoided.

A **Merocel sponge covering tape** (FDA-approved tape) can be used instead of the aluminum or copper foil. The Merocel is moistened with saline which consumes laser energy if it is struck (as above).

Unwrapped tubes have the following disadvantages:

They are highly combustible.

- **PVC tubes** are **more dangerous** because they produce hydrochloric acid and other toxic compounds.
- **Rubber tubes** are relatively **less dangerous** because they produce non-toxic compounds, so they are preferred.

Wrapped tubes with a metallic tape have the following disadvantages:

- **They do not offer cuff protection**.
- **They add thickness** to the tube; so, use 1-2 mm smaller size.

- **They are not an FDA approved** device.
- **Protection varies** with the type of the metal foil used.
- **Adhesive backing may ignite.**
- The reflective surface may **reflect laser** into the surrounding tissues.
- **Rough edges** may damage mucosal surfaces.
- **Airway obstruction** may occur from aspiration of **detached pieces of foil.**

3) Additional Protective Measures with Usage of the Tubes:

Because no tube is completely laser-proof, the following precautions should be taken:

1- **Decrease the inspired O_2 concentration** as low as possible and **avoid N_2O** as both O_2 and N_2O support combustion. Air (or helium)/O_2 25% mixture can be used. Some patients can tolerate 21% O_2 guided by a pulse oximeter.

2- **The cuff** should be filled **with saline** (rather than air) to dissipate the heat and it is better to use **saline dyed with methylene blue** to signal cuff rupture.

3- **Laser intensity and duration** should be **limited** as much as possible.

4- Isolation of the lesion with **saline-soaked pledgets (gauzes)** should be done to limit the risk of ignition.

5- **A source of water (60 mL syringe)** should be immediately available in cases of fire.

2. Protect the Patient's Skin, Teeth and Normal Tissues Adjacent to the Operative Field by using:

- **Wet gauze pads** or surgical sponges.
- **Water based lubricants** and **flame-resistant surgical drapes.**
- **Matt-finished or ebonized surgical instruments** rather than polished instruments to prevent reflection and inadvertent misdirection of the laser beam.

3. Evacuation of Toxic Vapors and Fumes (Laser Plume).

Efficient smoke evacuation must be maintained close to the operative site and operating room personnel must wear special (high filtration) masks.

4. Eye Protection.

- All the operating room personnel should wear **eye protection glasses** with side shields to protect the lateral aspects of the eyes (the glasses differ according to the type of laser used as each glass absorbs a specific wavelength according to the type of laser). These glasses have a color tint, which may make it difficult to monitor skin color changes (figure 19-5).
- A **warning sign** should be placed outside the operating room door whenever the laser is being used with extra glasses available for anyone entering the operating room.
- The patient's eyes should be taped shut and covered with wet eye packs.
- All windows should be covered with black window shades.



Figure 19-5: Laser protection glasses

Protocol and Management of Airway Fire:

The "4 Es" mnemonic may help to remember the steps of the protocol which are arranged in the following order:

1- **Extraction: Stop ventilation** and **remove the endotracheal tube.**

2- **Elimination: Turn off O_2** and **disconnect the circuit** from the machine.

3- **Extinguishing:** If the fire (flame) persists, **flood the surgical field** with **saline** immediately.
Once the fire stops, **ventilate with 100% O_2 by face mask and re-intubate.**

4- **Evaluation: Assess** airway damage, before patient awakening by:
- **Direct laryngoscopy.**

- **Fiberoptic or rigid** bronchoscopy (to also remove burnt debris).
- Consider **bronchial lavage** if needed.
- The decision to extubate the patient is based on the extent of burn, pulse oximeter readings, and arterial blood gases. The patients may need **mechanical ventilation and tracheostomy** in severe burns.
- The patient should be **monitored for 24 hours** after injury with serial chest examinations and oximetry.
- Inspired gases should be humidified.
- **Steroids** may be given to decrease laryngeal edema.
- **Antibiotics** may be given to treat superimposed infection.

Foreign Body Aspiration

It is an emergency condition especially in the pediatric population. It requires endoscopic removal using direct laryngoscopy and rigid bronchoscopy.

Preoperative Management:

- History of foreign body aspiration is usually short, but may be 2-3 weeks e.g., peanut.
- Clinical picture of foreign body inhalation should be assessed. The clinical picture differs according to the type of the obstruction:
  - **Acute obstruction** of the larynx; either:
    - **complete** resulting in **suffocation** (the patient struggle against his/her larynx) or
    - **incomplete (partial)** resulting in inspiratory **stridor** (if in the larynx) or inspiratory and expiratory stridor (if in the trachea) with **dry cough, wheeze, and hoarseness**. **Hypoxia** is usually present. **Bilateral decreased breath sounds** may occur.
  - **Valvular obstruction**: **Emphysema** of the affected lobe or segment may occur.
  - **Distal total obstruction: Distal consolidation and collapse** especially in the right lung (80%) may occur resulting in **infection and hypoxemia**.

- If **an irritant object** is aspirated e.g., a peanut, **reaction and edema** at the site of obstruction may occur.
- Chronically, retained airway foreign bodies often present with misdiagnosis of upper respiratory tract infections, asthma, or pneumonia.
- A child is considered **full stomach** because the excitement and distress will delay the stomach emptying. There are no benefits from waiting for stomach emptying.
- **Chest x- ray** is done (figure 19-6). It provides direct evidence if the aspirated object is radiopaque. If the aspirated foreign body is radiolucent, indirect evidence can be obtained by demonstrating hyperinflation of the affected lung (due to air trapping) and shifting of the mediastinum toward the opposite side on expiratory chest radiograph. Atelectasis occurs as a late finding, distal to the obstruction.
- **Premedication:**
  - **Administration of atropine (10-20 µg/kg i.v.) or glycopyrrolate (3-5 µg/kg i.v.)** is useful to decrease the likelihood of bradycardia from vagal stimulation during endoscopy.
  - **Dexamethasone** is frequently given prophylactically to decrease sub-glottic edema

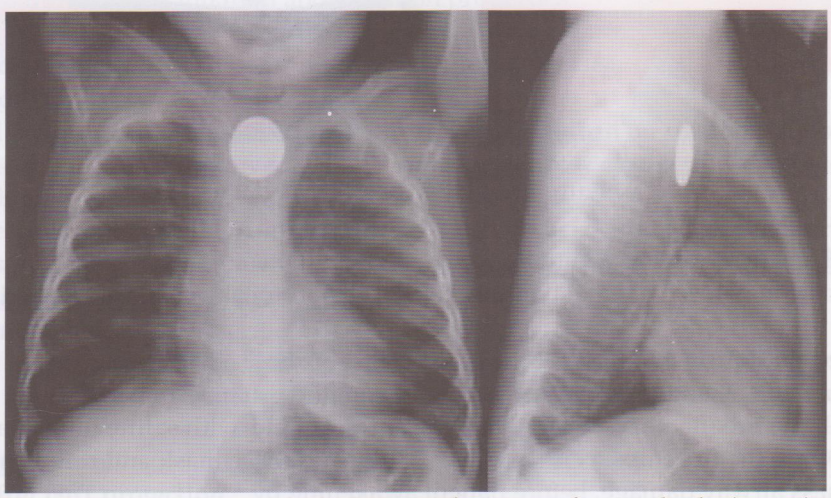


Figure 19-6: Plain chest x-ray PA and lateral views showing a foreign body (a coin) in the trachea

Intraoperative Management:

- **Inhalational induction** (by sevoflurane and oxygen) with the patient **breathing spontaneously** is usually mandatory due to presence of airway obstruction.
- The foreign body is removed by **laryngoscopy** and a McGill forceps (sometimes) or **rigid bronchoscopy** (usually).
- Total i.v. anesthesia may be used to maintain anesthesia during bronchoscopy to avoid exposing the surgeon to inhaled anesthetics and to maintain anesthesia during cessation of inhalational anesthesia.
- Spraying the larynx with a lidocaine solution is effective in preventing laryngospasm when endoscopic manipulation is performed.
- If complete airway obstruction arises, the foreign body needs to be extracted rapidly or **pushed down** usually to the right main-stem bronchus. This sometimes can be lifesaving; otherwise, **an emergency tracheostomy or cricothyrotomy** is performed.
- **Muscle relaxants (especially long acting) are often avoided** during bronchoscopy because:
  - Positive airway pressures could contribute to distal migration of foreign bodies, complicating their extraction.
  - If foreign bodies produce a ball-valve phenomenon, the use of positive-pressure ventilation of the lungs could contribute to hyperinflation and possibly pneumothorax.

Skeletal muscle paralysis produced with succinylcholine or short-acting nondepolarizing muscle relaxants may be required to remove the bronchoscope and foreign body if the object is too large to pass through the moving vocal cords. After completion of bronchoscopy, the patient is intubated with an endotracheal tube and extubated when the appropriate criteria of extubation are met.

- After the rigid bronchoscope is placed in the trachea, the anesthetic circuit can be attached to the breathing side port of the bronchoscope to maintain ventilation or an apneic oxygenation technique is used to maintain intermittent ventilation after removal of the endoscope when the oxygen saturation is decreased.
- All patients should be **observed closely** during the recovery period for **airway edema** and respiratory compromise.

Postoperative Management:

- **Postoperative laryngeal stridor** is common; therefore, the patient should be closely observed for 12 hours in a high dependency unit.
- **Nebulized racemic epinephrine** is useful in treating **post-intubation croup**.
- **Chest radiographs** should be obtained after bronchoscopy to **detect atelectasis or pneumothorax**.
- **Postural drainage and chest percussion** enhance clearance of secretions and decrease the subsequent risk of infections.

Head and Neck Cancer Surgery

Examples of head and neck surgeries are laryngectomy, glossectomy, pharyngectomy, parotidectomy, hemi-mandibulectomy and radical neck dissection.

Anesthetic Problems:

- Type of patients.
- Airway obstruction and difficult intubation.
- Increased blood loss.
- Increased temperature loss.
- Venous air embolism.
- Special surgical problems.
- Postoperative care of the airway.
- Postoperative complications.

Preoperative Management:

- Type of patients: Patients are usually **heavy smokers or alcoholics** (as etiological factors); therefore, careful preoperative assessment for **cardiac** (e.g., coronary artery diseases), **respiratory** (e.g., chronic obstructive airway diseases) or **hepatic** function should be done.
- **Preoperative airway assessment** is important for detection of obstruction by the tumor itself or by preoperative irradiation resulting in glottic edema and fibrosis. Both fibrosis and edema may cause partial or severe obstruction resulting in stridor at rest. These patients may need **preoperative tracheostomy**

under local anesthesia. Personnel and equipment for emergency tracheostomy should be always available.

- **There is an increased blood loss;** so, ▫ two large bore i.v. lines should be secured and
  ▫ cross matched blood should be available.

Premedications:

Sedatives and opioids should be avoided if there is airway obstruction.

Intraoperative Management:

Induction and Intubation:

a- Severe obstruction (stridor at rest) needs **preoperative tracheostomy under local anesthesia.**

b- Moderate obstruction (may progress to severe obstruction on loss of consciousness) needs **awake fiber optic** intubation in cooperative patients.

c- Mild obstruction in uncooperative patients needs **inhalational induction** and intubation at deep anesthetic levels.

d- If there is **no risk of obstruction,** induction with a sleeping dose of an i.v. agent such as thiopentone can be done. If easy mask ventilation, give suxamethonium to facilitate intubation.
If difficult mask ventilation, deepen anesthesia by halothane for intubation.

N.B.: ▫ I.v. agents are absolutely contraindicated if there are any doubts regarding the patient's ability to maintain a patent airway after loss of consciousness.
▫ All equipment for difficult intubation should be available.

Monitoring:

Besides the standard monitors:

- Invasive monitors (central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, and invasive arterial blood pressure) are usually applied due to marked blood loss and due to the associated respiratory and cardiac diseases.
- Temperature.
- Monitors for **venous air embolism** e.g., precordial or esophageal stethoscope and trans-esophageal echocardiography.

Maintenance:

N_2O/O_2, volatile agents, opioids, muscle relaxants, and controlled ventilation are usually used.

Intraoperative Problems:

1. Increased Blood Loss which may necessitate controlled hypotension and proper fluid and blood transfusion management.

2. Increased Temperature Loss: due to lengthy surgeries, large incision, increased blood loss which necessitates warm fluids, warm blankets…etc.

3. Increased Risk of Venous Air Embolism especially in the head up position.

4. Special Surgical Problems:

a. **During Tracheal Transection:** (tracheostomy is usually a part of head and neck surgery).

- 1st ventilate the patient's lung with 100% O_2 for 2 min.
- **Compatible connections for a non-kinkable (reinforced) sterile tube** should be available before the trachea is divided.
- The patient is then disconnected, cuff deflated and the endotracheal tube is withdrawn to the larynx then the trachea is divided.
- Place a **new endotracheal tube** into the trachea rapidly; **ensure its position by capnography** and hearing the breath sounds then the tube is secured firmly. A laryngectomy tube can be used which decreases the risk of slipping (figure 19-7).
- An increase in the peak inspiratory pressure immediately after the tracheostomy usually indicates a mal-positioned tube, bronchospasm, or debris in the trachea.

b. **During Pharyngo-Laryngectomy:**

- **Mobilization of the stomach up is usually needed**. This is done by one of 2 surgical approaches either: ▫ the stomach is passed through a mediastinal tract by blunt dissection, or
  ▫ the stomach is mobilized through a thoraco-abdominal incision.
- **Injury of the trachea** may cause difficult ventilation and mediastinal emphysema.

c. **During Radical Neck Dissection:**

- **Carotid sinus and stellate ganglion manipulation** (right side > left side) result in a **vagal reflex** which causes hypotension, bradycardia, and arrhythmias up to arrest. This is treated by:

- Stopping manipulations.
- Blocking of the carotid sinus nerves by local infiltration of the carotid sheath with lidocaine.
- I.v. atropine.

• The surgeon may request the omission of muscle relaxants to identify certain nerves e.g., spinal accessory or facial nerves by direct stimulation to preserve them.
• **Cerebral perfusion pressure** may be severely **compromised** when the tumor involves:
- The carotid artery leading to a decrease in cerebral arterial pressure.
- The jugular vein leading to an increase in cerebral venous pressure.

• Injury of the pleura leading to **pneumothorax**.

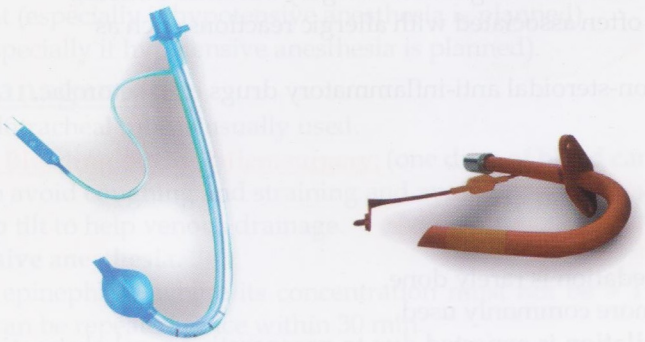


Figure 19-7: Laryngectomy tubes; PVC tube (left) and red rubber tube (right)

Postoperative Management:

1. Postoperative Care of Airway:

• Change the tracheal tube by laryngectomy or tracheostomy tube.
• Provide humidified 40% O_2: air mixture.
• Frequent suction of the trachea.
• Nutrition by naso-gastric tube to protect the airway.

2. Postoperative Complications:

• Exclude lung collapse and pneumothorax by chest x-ray and auscultation.
• Bilateral neck dissection may cause postoperative hypertension and loss of hypoxic drive due to denervation of the carotid sinuses and bodies.

Nasal and Sinus Surgery

Anesthetic Problems:

• Increased blood loss; so, nasal preparation, head up, and controlled hypotension are needed.
• Difficult mask ventilation.
• Associated allergic reactions.
• Pharyngeal pack.
• Eye protection.

Preoperative Management:

Preparation of the Nose with Local Anesthetics and Vasoconstrictors:

• Lidocaine 2% with epinephrine 1: 100 000- 1: 200 000 solution.
• Cocaine 4-10% as an analgesic and vasoconstrictive agent (maximal intra-nasal dose 1.5-3 mg/kg) administered by spray, paste gel, soaked swabs, or infiltration.

Preparation of the nose is performed by:

1. **Curtiss Simplified Moffatt's Method:**

• The patient lies supine with his head fully extended over the end of the trolley and supported by an assistant. A round-ended angulated needle is inserted with its tip directed along the floor of the nose. When the angle of the needle is reached, redirect **the tip towards the roof** of the nose and 2 mL of local anesthetic solution are to be deposited when the tip has made contact. The procedure is repeated in the

other nostril. The patient remains in this position for 10 min and asked to sit upright and spit out any residual solution which trickles into the pharynx.

• In anesthetized patients, another modification of Moffatt's methods can be applied. Instillation of 10 mL of diluted cocaine into each nostril with the head extended is performed after placement of a gauze throat pack which holds the solution in the nose for obtaining a maximum effect.

2. **Packing the Nose** with gauze or cotton tipped applicators soaked with local anesthetics and left for 10 min is also used.

Advantages of Moffatt's method over nasal packing: • Minimal patient discomfort during preparation.
• Lower risk of cocaine toxicity.

Nasal preparation for nasal polypectomy and diathermy of turbinates are omitted by many surgeons because nasal mucosa will shrink to a degree that surgery becomes difficult.

Presence of nasal polyps is often associated with allergic reactions such as
- bronchial asthma and
- allergy to aspirin and non-steroidal anti-inflammatory drugs e.g., ketorolac.

Premedications:

Sedatives are essential.

Intraoperative Management:

Choice of Anesthesia

a. **Local infiltration:** with sedation is rarely done.

b. **General Anesthesia:** is more commonly used.

• **Difficult face mask ventilation** is expected due to preoperative nasal obstruction e.g., polyps, deviated septum. Oral airway during mask ventilation is very helpful.

• **Induction: Smooth induction** is preferred to avoid coughing and straining because they increase venous congestion resulting in increased bleeding.

N.B.: Do not spray the larynx with local anesthetic before intubation to allow full return of laryngeal reflexes on recovery.

• **Intubation** is performed by a **non-kinkable cuffed** endotracheal tube either oral RAE tube or Mallinckrodt critical care tube.

• **The posterior pharynx should be packed** by a two-inch ribbon gauze to absorb blood and decrease the risk of blood aspiration. The presence of the pack should be marked by writing on the strapping which secures the tube or over patient's forehead to remind the anesthesiologist to remove it at the end of surgery. Tying the pack to the endotracheal tube is another alternative.

• **The patient's eye should be taped** closed to **avoid corneal abrasion** due to the proximity of the surgical field. One exception to this is during **endoscopic sinus surgery**, when the surgeon may wish to periodically check for eye movement during dissection due to the close proximity of the sinuses to the orbit.

• **Surgeries to control epistaxis** (e.g., ligation of the maxillary artery) are anesthetized with the same anesthetic management of post-tonsillectomy bleeding. Patients are usually elderly hypertensive.

Patient Position: 10 degree head up.

Monitoring:

Besides the standard monitors, ECG is used to detect arrhythmias which occur commonly during face surgery.

Maintenance:

• Controlled ventilation with muscle relaxation is strongly recommended due to the potential neurological or ophthalmic complications that may occur if the patient moves during sinus instrumentation.

• Controlled hypotension may be required.

Extubation:

• **Smooth extubation** may be used to avoid coughing and straining, but this may increase **the risk of aspiration**; so, **awake extubation** in the lateral position **is the usual.**

• Removal of the pack then suction of the pharynx are performed while the head is in lateral position.

• An oral airway should be placed before removal of the endotracheal tube to provide a patent airway in the presence of surgical nasal packing.

N.B.: Cannulated nasal packing may be used to allow patency of the airway.

Ear Surgery

Anesthetic Problems:

1- Bleeding with microsurgery.
2- Effect of N_2O.
3- Identification of facial nerve.
4- Postoperative nausea and vomiting.
5- Bandaging of the ear.

Preoperative Management:

Premedications:

- Sedatives are important (especially if hypotensive anesthesia is planned).
- Atropine is omitted (especially if hypotensive anesthesia is planned).

Intraoperative Management:

A non-kinkable oral endotracheal tube is usually used.

1- Measures Decreasing Bleeding during Microsurgery: (one drop of blood can obscure the field).

- **Smooth induction** to avoid coughing and straining and avoid hypertensive response to intubation.
- 10-15 degree **head up** tilt to help venous drainage.
- **Controlled hypotensive anesthesia.**
- Local infiltration of epinephrine where its concentration must not be > 1: 100 000. Only 10 mL are given at a time which can be repeated twice within 30 min.

2- The Effect of N_2O on the Middle Ear:

Normally, there is no effect of N_2O on the middle ear due to presence of a patent Eustachian tube. In chronic inflammation such as otitis media or sinusitis, the Eustachian tube will be obstructed and the middle ear cavity becomes closed. Therefore, N_2O will diffuse rapidly into the middle ear faster than nitrogen (N_2) leaving it (the major component of air) as N_2O is 34 times more soluble in blood than N_2, resulting in an increased pressure which is maximum about 4 min after induction. This causes hearing loss and rupture of the tympanic membrane.

During tympanoplasty, the middle ear is open to the atmosphere and there is no pressure build-up. Once the surgeon has placed a tympanic membrane graft, the middle ear becomes a closed space again. N_2O can diffuse into this space leading to an increase in the middle ear pressure with displacement of the graft. Also, discontinuing N_2O after graft placement will create a negative middle ear pressure; so, the graft may be displaced also.

N_2O is either entirely avoided during tympanoplasty or discontinued prior to graft placement by 10-15 min.

3- Identification of Facial Nerve during Surgery:

This is performed by **a peripheral nerve stimulator.** Theoretically, this needs a non-paralyzed patient, but actually, most anesthesiologists use muscle relaxants.

Recovery:

- **Ear bandaging at the end of surgery causes** movement of the head. It must be anticipated and supervised by the anesthesiologist. **Deep extubation** is advised to avoid gagging and coughing on the endotracheal tube which increases bleeding.
- Ear surgery, especially if **labyrinthine function** is disturbed, produces **postoperative vertigo and vomiting;** so, anti-emetics are essential.
- **Assess facial nerve function postoperatively.**

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Web Sites:

- http://www.gov.uk/cjd.index.htm

OPHTHALMOLOGY

20

• Intraocular pressure. • Oculomedullary reflexes. • Systemic effects of ophthalmic medications. • General anesthesia of ophthalmic surgery. • Traumatic (penetrating, open) eye injury. • Retinal surgery.	• Regional anesthesia for ophthalmic surgery. • Extra-ocular surgery. Squint (strabismus) surgery. Examination under anesthesia. Dacro-cysto rhinostomy. • Postoperative corneal abrasion.

Patients who present for eye surgery are frequently at the extreme ends of age. Both pediatric and geriatric anesthesia present special problems.

Intra-Ocular Pressure (IOP)

Normal IOP equals **10-20 mm Hg** (mean = 15 mm Hg). IOP is considered **abnormal** when **higher than 25 mm Hg**.

IOP transiently changes with posture (decreases in the upright position and increases in the supine position by 2-4 mm Hg), blinking (increases IOP 5 mm Hg), squeezing or squinting (increases IOP 26 mm Hg), coughing, straining, or vomiting. These transient changes are normal and are well tolerated in normal intact eyes, but these temporary changes are not tolerated in patients with low ophthalmic artery pressure such as controlled hypotension, atherosclerosis of retinal artery (resulting in decreased retinal perfusion and retinal ischemia) and when the globe is open during surgery (resulting in vitreous extrusion, hemorrhage, or lens prolapse).

Factors Affecting IOP:

1- External Pressure on the Eye: increases IOP such as:

- Injection of a large local anesthetic volume into the orbit (transiently elevates IOP for 2-3 minutes).
- A tightly applied anesthetic face mask.
- A surgical retractor.
- Retrobulbar hemorrhage.
- Improper prone position.

2- Vascular (Choroidal) Volume: is determined by the balance of arterial flow and venous drainage.

a. Central Venous Pressure (CVP):

An **elevated CVP** increases ocular vascular pressure and decreases aqueous drainage resulting in an **increased IOP** such as in:

- Valsalva maneuver-like as airway obstruction, coughing, vomiting and bucking on the endotracheal tube. This increases the IOP 30-40 mm Hg.
- Mechanical ventilation that increases the mean intra-thoracic pressure (it can be compensated by the control of $PaCO_2$).
- Trendelenburg position.

A fall in the CVP decreases IOP such as in:
- deep inspiration.
- head up (anti-trendelenburg) position.

b. Arterial Blood Pressure:

Ocular blood vessels have autoregulation as that present in cerebral and coronary blood vessels. **An increased arterial blood pressure** above the autoregulation ranges **increases the IOP** such as in:

- Valsalva maneuver.
- Straining in an inadequately relaxed patient.
- Laryngoscopy and intubation (pressor response).
- Trendelenburg position.

A decreased arterial blood pressure below the autoregulation range **decreases the IOP**. Decreased systolic arterial blood pressure < 85 -90 mm Hg causes a marked decrease in the IOP while at 50-60 mm Hg, the IOP is zero i.e., atmospheric.

c. $PaCO_2$:

An increased $PaCO_2$ leads to vasodilatation of the choroidal vessels causing **an increase in the IOP** e.g., during hypoventilation.

A decreased $PaCO_2$ leads to vasoconstriction of the choroidal vessels causing **a decrease in the IOP** e.g., during hyperventilation.

d. PaO_2:

An increased PaO_2 has no effects while **a decreased PaO_2** results in vasodilatation of the ocular vessels causing **an increase in the IOP**.

3- Aqueous and Vitreous Volumes:

They are determined by the balance of production and drainage of aqueous. They are less important during surgery. Their reduction is important in treatment of glaucoma (pathological increase in IOP due to decreased aqueous drainage) results in decreased IOP.

Aqueous and vitreous volumes can be reduced by:

- Osmotic dehydrating agents such as ▫ mannitol 1-1.5 g/kg i.v. infusion.
  ▫ sucrose 50% 1 g/kg i.v. infusion.
- Acetazolamide 500 mg i.v. (a carbonic anhydrase inhibitor) that inhibits the Na^+ pump which results in decreased aqueous production and increased drainage.

N.B.: Aqueous Humor Formation and Drainage:

Its volume is 0.3 mL. It is formed in the posterior chamber. It circulates through the pupil to the anterior chamber, then to the trabeculated spaces of Fontana. The aqueous then passes to the canal of Schlemm, then to the episcleral veins. Finally, the aqueous reaches the cavernous sinus or jugular venous system (figure 20-1).

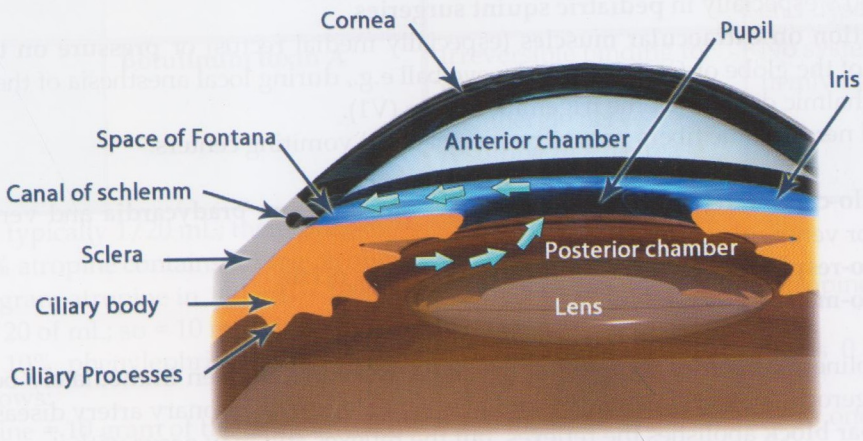


Figure 20-1: Aqueous humor formation and drainage

Effect of Anesthetic Drugs on IOP:

1. Inhalational Agents:

Nitrous oxide slightly decreases or has no effect on the IOP. Halothane, isoflurane, enflurane (more than others), and sevoflurane **decrease IOP** because:

- They decrease arterial blood pressure resulting in decreased choroidal volume.
- They relax extraocular muscles resulting in decreased wall tension.
- They cause miosis which increases aqueous drainage.
- They decrease aqueous formation.

2. Intravenous Agents:

Thiopentone, etomidate, benzodiazepines, and propofol (less) **decrease IOP**. Opioids decrease IOP, but if respiratory depression occurs, $PaCO_2$ increases, PaO_2 decreases or/and postoperative nausea and vomiting may occur with a resultant increase in the IOP.

Ketamine increases IOP due to the elevated blood pressure and increased tone of the extraocular muscles. It also causes nystagmus and blepharospasm; therefore, it is contraindicated in eye surgeries.

3. Muscle Relaxants:

• Depolarizing muscle relaxants such as **succinylcholine transiently increase the IOP** by 5-10 mm Hg within 1-4 minutes after i.v. administration, followed by a return to baseline in about 7 minutes due to intraocular vasodilation and increased tone of extraocular muscles.

Defasciculation by non-depolarizing muscle relaxants may abolish the effect of succinylcholine on IOP, but some authors deny this.

Succinylcholine causes:

- False measurements of IOP during examination under general anesthesia in glaucoma patients which may lead to unnecessary surgery.
- Extrusion of ocular contents during open eye injury.
- Abnormal forced duction test for 20 min; this test evaluates the cause of extraocular muscle imbalance or may affect the type of strabismus surgery performed.

• **Nondepolarizing muscle relaxants** have **no effect or may decrease IOP** by reduction in the tone of extraocular muscles.

4. Anticholinergics:

Scopolamine > atropine > glycopyrrolate cause **a slight increase in the IOP** because mydriasis causes obstruction of the aqueous drainage. They are contraindicated in glaucoma patients.

Atropine i.v. or topical increases the IOP, but i.m. 0.4 mg as premedication does not increase the IOP because only 0.0001 mg is absorbed by the eye.

Glycopyrrolate is the safest because it is a quaternary ammonium compound (bulky) and does not cross the blood brain barrier.

Oculo-Medullary Reflexes

They include **oculo-cardiac**, oculo-respiratory, and oculo-metric reflexes

Incidence: 50-80% especially in **pediatric squint surgeries**.

Stimulus: **Traction on extraocular muscles** (especially medial rectus) or **pressure on the eye ball** either from the front of the globe or from behind the eye ball e.g., during local anesthesia of the eye.

Afferent: Ophthalmic division of the trigeminal nerve (V1).

Efferent: Vagal nerve. Some fibers pass to respiratory and vomiting centers.

Response:

- In the **oculo-cardiac reflex**, **heart arrhythmias** ranging from **bradycardia** and ventricular ectopy to sinus arrest or ventricular fibrillation may occur.
- In the **oculo-respiratory reflex, respiratory arrest** may occur.
- In the **oculo-metric reflex,** nausea may occur.

Prophylaxis:

- An anticholinergic such as **atropine or glycopyrrolate** i.v. is given immediately before surgery, but they are dangerous in elderly patients who have some degree of coronary artery disease.
- **Retro-bulbar block** abolishes the reflexes, but the reflexes still may occur with it.
- **Deep inhalational anesthetics** can be used, but the reflexes may still occur with them.
- Hypercapnia should be avoided because it appears to sensitize the reflexes.

Management:

- Immediate notification of the surgeon and cessation of stimulation are important.
- Confirmation of adequate ventilation, oxygenation, and depth of anesthesia are essential.
- I.v. atropine 0.01 mg/kg if conduction disturbances persist.
- In resistant episodes, infiltration of the rectus muscle with local anesthetics is done.

N.B.: The reflexes fatigue (i.e., self-extinguish) with repeated traction on the extraocular muscles.

Systemic Effects of Ophthalmic Medications

Topically applied eye drops are absorbed by vessels in the conjunctival sac and the nasolacrimal duct mucosa at a rate intermediate between absorption after intravenous and subcutaneous injection especially in children and elderly who are more susceptible to eye surgeries.

Finger pressure on the inner canthus for a few minutes after instillation of eye drops will impede absorption by occluding the nasolacrimal duct.

Ophthalmic Use	Drug	Action	Systemic Effects
Miosis (pupillary constriction)	**Acetylcholine**	A cholinergic agonist	Bronchospasm, bradycardia and hypotension.
Glaucoma (they decrease IOP)	**Echothiophate (*Phospholine iodide*)**	An irreversible cholinesterase inhibitor; inhibition persists up to 3-7 weeks after discontinuation of the drug.	As acetylcholine + prolongation of the action of succinylcholine (for 20-30 minutes) and ester local anesthetics.
	Timolol (*Timoptic*)	A beta blocker	As acetylcholine.
	Acetazolamide	A carbonic anhydrase inhibitor.	Diuresis with dehydration, hypokalemia, and metabolic acidosis.
	Mannitol	An osmotic diuretic.	Initial circulatory overdose.
Mydriasis (pupillary dilatation) **and ocular capillary decongestion** (by vasoconstriction)	**Atropine or scopolamine**	An anticholinergic.	Central anticholinergic syndrome.
	Epinephrine or phenylephrine	A sympathomimetic.	Tachycardia, hypertension, and nervousness.
	Cyclopentolate	An anticholinergic.	Disorientation, psychosis, convulsions, and dysarthria.
Squint	**Botulinum toxin A**	Irreversible binding to receptor site on the cholinergic nerve resulting in a decrease in the muscle power.	No systemic effects as it firmly bound to tissues.

N.B. One drop is typically 1/20 mL; therefore,

- One drop of 1% atropine contains 0.5 mg atropine which is explained as follows:

1% atropine = 1 gram atropine in 100 mL = 1000 mg atropine in 100 mL = 10 mg atropine in one mL and as one drop is 1/20 of mL; so = 10 mg/20 drops = 0.5 mg/drop.

- One drop of 10% phenylephrine contains 5 mg phenylephrine (the i.v. dose is 0.5 mg) which is explained as follows:

10% phenylephrine = 10 gram of the drug in 100 mL = 100 mg drug in one mL and as one drop is 1/20 of mL; so, = 100 mg/20 drops = 5 mg/drop.

Intra-Ocular Surgery

The choice between general anesthesia and local anesthesia should be made jointly by the patient, the anesthesiologist, and the surgeon. The majorities of patients who undergo elective ophthalmic procedures are elderly and have multiple comorbid conditions which necessitate a specific type of anesthesia.

General Anesthesia for Ophthalmic Surgery

Aim:

1- A moderate decrease in the IOP to prevent expulsion of the eye content via the surgical incision because if the IOP is increased, a sudden reduction in pressure on incision may cause expression of contents or expulsive hemorrhage.

2- Complete immobility of the eye especially for microsurgical procedures.

3- Maintaining the hemodynamic stability of the patients as usual.

Indications of General Anesthesia: (are the same as **contraindications of local anesthesia**)

1- **Patient refusal** of local anesthesia of the eye.

2- Eyes liable for complications e.g., **diabetic patients**.

3- **High myopia with axial length > 26 mm** as there is increased risk of perforation; otherwise, single medial canthus injection, the sub-Tenon approach, or topical anesthesia are used.
4- **Open eye injury** because the pressure from injecting local anesthetic solution behind the eye may cause extrusion of intra-ocular content through the wound.
5- **Children and young patients** are more suitable for general anesthesia while elderly patients are more suitable for local anesthesia.
6- Patients with **mental disability**.
7- Patients with **physical disability** i.e., patients unable to lie flat and remain motionless up to the time of surgery.
8- **Lengthy surgeries** such as vitreo-retinal procedures.
9- **An aphakic patient** i.e., with a single functioning eye.
10- Patients with an infected eye.
11- Patients with **coagulopathies or on warfarin therapy**; local anesthesia can be safely done if preoperative INR value is in the therapeutic range i.e., < 2.5 otherwise, sub-Tenon approach or topical anesthesia can be used.

Anesthetic Problems:

1- Type of patients who are usually at extreme ends of age i.e., pediatric or elderly patients.
2- Factors which increase the IOP e.g., straining and coughing should be avoided.
3- The patient is away from the anesthesiologist.
4- Postoperative vomiting is common.
5- Postoperative analgesia is important.

Preoperative Management:

Patients are at the extreme ends of age. They are either:

- **Pediatrics:** who may be suffering from congenital disorders e.g., Down's syndrome.
- **Geriatrics:** who may be suffering from systemic disorders e.g., hypertension or ischemia.

Patients may be apprehensive especially if there is a possibility of permanent blindness.

Premedications:

- **Sedatives** e.g., oral diazepam 0.1 – 0.2 mg/kg is usually used, but the dose should be reduced in elderly patients.
- **Anticholinergics**, especially in pediatrics, are recommended to decrease the oculo-cardiac reflex and decrease saliva if laryngeal mask is used.
- **Antiemetics** e.g., metoclopramide 10 mg i.v. or ondansetron is commonly used to avoid postoperative vomiting.

Intraoperative Management

Induction: **Smooth induction** is important to avoid increased IOP.

- Avoid pressor response to intubation. It is discussed in the chapter of "Airway Management".
- Avoid coughing and straining on intubation.
- Induction agents:
  - Propofol is of choice because it causes less postoperative nausea and vomiting.
  - Thiopentone is a good alternative.
  - Etomidate is of choice in elderly and unfit patients as it decreases the IOP and maintains cardiovascular stability, but care should be taken for:
    - Occurrence of unpredictable generalized myoclonus which increases the IOP; so, it is avoided in open eye injury except if rapid and complete prior muscle relaxation is guaranteed.
    - As it is painful on injection, it causes stress; therefore, it should be given in a large vein with 1-2 mL lidocaine 2%.
  - **Ketamine is avoided as it increases the IOP.**
- **Suxamethonium:** provides **an ideal condition** for intubation with a minimal risk of coughing or straining because it produces intense muscle relaxation. It causes a transient increase in IOP which disappears by the time the surgery starts.
- Non-depolarizing muscle relaxants are a good alternative.
- Intubation:
  - **Laryngeal mask airway** is routinely used unless there is a no contraindication (an armored tube laryngeal mask is preferred). It can be used with controlled ventilation.

Advantages: Easily inserted.
No pressor response of laryngoscopy and intubation.
No postoperative coughing or straining of laryngospasm (which is more common with intubation).

Disadvantages: Not suitable for patients who are at a risk of aspiration e.g., open eye injury, morbidly obese patients… etc.

- Endotracheal tube is used if laryngeal mask airway is contraindicated.

• Taping the non-operative eye is essential.

Monitoring:

Besides the standard monitors,

• Pulse oximetry: because the anesthesiologist is away from the patient's airway.
• ECG with audible beep to detect oculo-cardiac reflex.
• End tidal CO_2 to differentiate malignant hyperthermia from increased body temperature by drapes and can early detect inadequate ventilation due to malpositioned laryngeal mask airway.
• Body temperature: In contrast to most pediatric surgeries, infant body temperature often increases during ophthalmic surgeries due to: head to toe draping and insignificant body surface exposure.
• Continuous monitoring for breathing circuit disconnection or unintentional extubation.
• Peripheral nerve stimulator to guarantee that no cough, straining, or patient movement occurs.

Maintenance:

• **Controlled ventilation** is used to produce moderate hyperventilation. Mechanical ventilation can be used with laryngeal mask airway as long as **peak airway pressure is < 15-20 cmH_2O** to decrease the risk of gastric insufflation and aspiration.
• Non-depolarizing muscle relaxants are given before the action of suxamethonium ends to ensure that no coughing or straining occurs, with the help of **a peripheral nerve stimulator**.
• 15° head up tilt is usually needed.
• Advantages of controlled ventilation (over spontaneous ventilation):
1- To guarantee that no coughing or straining occurs.
2- To ensure decreased $PaCO_2$ resulting in decreased IOP.
3- To allow a lighter plane of anesthesia to maintain cardiovascular stability and ensure rapid recovery.

Intraoperative Anesthetic Problems:

• Anesthetic problems of traumatic eye injury.
• Anesthetic problems of retinal surgery.

Both are discussed later.

Extubation:

Smooth extubation is needed by one of the following methods:

• Deep extubation with inhalational agents or propofol 30-40 mg 1 minute prior to extubation.
• Lidocaine either i.v. 1.5 mg/kg or as a spray for vocal cord 1-2 minutes before extubation.

This technique is not suitable for patients at increased risk of aspiration.

N.B.: Modern suture materials and wound closure techniques by using the microscope decrease the risk of postoperative wound dehiscence. It is the surgeon's responsibility to ensure water tight closure of the wound.

Postoperative Management:

1- Postoperative Vomiting:

It is common due to vagal stimulation especially after strabismus surgery. Vomiting increases IOP and may increase the risk of aspiration; therefore, pre-or intra-operative antiemetics are given.

2- Postoperative Analgesia:

It is important because pain increases IOP; therefore, pethidine i.v. 15-25 mg or papaveretum (analgesic + antiemetic) is given.

Traumatic (Penetrating, Open) Eye Injury

The IOP is equal to the atmospheric pressure (i.e., zero) as the eye is opened to the outside, but increased choroid and vitreous humor volume may cause extrusion of the eye content via the wound. Most patients have **full stomach**. The patients must be considered to have a full stomach if the injury occurred within 8

hours of the last meal even if the patient has not eaten for several hours since the injury, because gastric emptying is delayed by the pain and anxiety following the trauma.

Anesthetic Management:

Only general anesthesia is used when regional anesthesia is contraindicated.

The anesthetic management of traumatic eye injury is the same as that discussed before with general anesthesia **except**:

Premedication:

- Avoid aspiration by:
  - Metoclopramide i.v. 10 mg repeated every 2-4 hours till surgery.
  - H_2 blockers as cimetidine 300 mg i.v., ranitidine 50 mg i.v., or famotidine 20 mg i.v.
  - Antacids just before induction as their duration of action is 30-60 min only, but they increase gastric volume.
- Avoid gastric evacuation by nasogastric tubes as this precipitates coughing, and straining which increase IOP.

Induction:

Modified rapid sequence induction is mandatory with the following precautions:

- **Avoid pressure on the injured eye with the face mask** during preoxygenation; the eye can be patched with a shield.
- The stress response of intubation should be blunted by β-blockers, Ca^{++} channel blockers, lidocaine or midazolam. Avoid spraying the larynx with local anesthetics as this may blunt the protective reflexes.
- Cricoid pressure (poorly applied cricoid pressure may block venous drainage of eye).
- The use of the laryngeal mask should be avoided due to the possibility of a full stomach.

Modified rapid sequence induction can be done by:

a- **Non-depolarizing muscle relaxants:** The onset can be fastened by either:

- administering a relatively larger dose, but this prolongs muscle relaxation and increases side effects:

Drug	Dose	Onset	Problems due to the relatively large doses
Rocuronium	0.8-1.0 mg/kg	60-70 sec	Prolonged muscle relaxation (45-60 minutes)
Vecuronium	0.2 mg/kg	60-90 sec	Prolonged muscle relaxation
Pancuronium	0.15-0.2 mg/kg	90 sec	Prolonged muscle relaxation and tachycardia
Cis-atracurium	0.4 mg/kg	60-90 sec	Prolonged muscle relaxation (may exceed 60 minutes)
Atracurium	1.5 mg/kg	60-90 sec	Excessive histamine release with hypotension and tachycardia.

or • giving a priming dose (a small dose is administered at first followed by the full dose within 5 minutes) without increasing the dose of nondepolarizing muscle relaxant.

b- **Suxamethonium**: Some prefer avoiding it as it produces a transient increase in IOP in open eyes, but the effect of laryngoscopy and intubation on IOP is much greater more than the effects of suxamethonium. Therefore, measures to decrease the pressor response of intubation can abolish the effect of suxamethonium; so, it can be used especially if difficult intubation is suspected.

Extubation:

Awake extubation in the lateral position is preferred. Although awake extubation can increase the IOP, the risk of aspiration during deep extubation is greater. The stomach can be emptied by a naso-gastric tube while the patient is still paralyzed.

Retinal Surgery

Anesthetic Problems:

1- The type of Patients:

They are usually young patients who are liable to become uncomfortable and restless if they lie on a hard operating table for too long; therefore, **general anesthesia is preferred**.

If the patient is medically compromised or the procedure is of short duration, local anesthesia is used.

2- Darkness of the Operating Room:

Fundal examination, vitrectomy, and laser surgeries are carried out in a **dark room**. The anesthesiologist should ensure that there is sufficient light to conduct anesthesia safely and goggles against laser should be worn.

3- Oculo-Cardiac Reflex:

It is common, especially during banding with scleral buckle.

4- Intraoperative Gas Bubble Effect:

At the end of retinal detachment, the surgeon often injects a bubble of air (lasting for 5 days) or sulfur hexafluoride (lasting for 10 days) into the posterior chamber to tamponade the retina. These are then absorbed by gradual diffusion through the adjacent tissues and into the blood stream. Therefore,

a- **N_2O must be discontinued at least 15 min before injection of the gas bubble** and anesthesia is continued by air/O_2 and additional volatile agents or total intravenous anesthesia (TIVA) because N_2O will enter the gas bubble at a rate more than N_2 (the major component of air) or sulfur hexafluoride leave the bubble i.e., N_2O equilibrates more rapidly because it is more soluble than N_2 and sulfur hexafluoride in blood resulting in an increased bubble size. This increases IOP. 70% N_2O can triple the size of 1 mL bubble which doubles the IOP within 30 minutes.

At the end of the anesthesia, N_2O diffuses out more rapidly decreasing the size of the gas bubble. This can precipitate another retinal detachment.

Also, N_2O should be avoided during subsequent anesthesia of these patients until the bubble is absorbed; 5 days for air, 10 days for sulfur hexafluoride (SF6).

b- As soon as there is sufficient recovery from anesthesia, the patient is turned 180° to the prone position, so that the bubble exerts upward pressure on the area of the retinal detachment.

Recently, the use of silicone oil as a heavy medium to roll the retina back into position after specific types of detachment or giant retinal tears eliminates the need for 180° longitudinal rotation of the eye after surgery.

Regional (Local) Anesthesia for Ophthalmic Surgery

Applied Anatomy

- **The orbit:** is pyramidal (cone) shaped with its base at the orbital opening and its apex pointing to the optic foramen. The orbit is formed of the globe, extraocular muscles, and loose connective tissue through which local anesthetic solutions can easily spread.
- **The globe:** lies in the anterior part of the orbit and stay high and lateral in the orbital cavity; therefore, needle penetration is achieved either medially or infero-laterally where the gap between the globe and orbital wall is greatest.
- **The sclera:** forms the fibrous bulk of the globe. It is 1 mm thick and tough, but can be penetrated by sharp needles.
- **Tenon's capsule or fascia:** is a membrane that lies superficial to, and encloses the sclera and lies directly underneath the conjunctiva. It is easily recognized as it is white and avascular, unlike the vascular sclera below. The space between the Tenon capsule (superficial) and sclera (deep) is called **sub-Tenon space** where sub-Tenon block is performed.
- **Extra-ocular muscles:** There are 6 extra-ocular muscles; **4 recti muscles** form the muscle "cone" which encloses the sensory and motor nerves, ciliary ganglia, optic nerve, retinal artery and vein. There are also **2 oblique muscles**. The movement of the globe is controlled by the 6 extraocular muscles. The 4 recti muscles form a fibrous origin called the common tendinous ring at the apex of the cone.
- **Nerve supply of the extraocular muscles:**
  - The lateral rectus is innervated by the abducent nerve (6th cranial).
  - The superior oblique is innervated by the trochlear nerve (4th cranial).
  - All the rest extraocular muscles are innervated by the oculomotor nerve (3rd cranial) i.e., $(LR_6SO_4)_3$.

The motor nerves which supply extraocular muscles emerge from the skull through the superior orbital fissure outside and inside the common tendinous ring (figure 20-2).

- **Squeezing and Closing the Eyelids:**

Eyelids are controlled by orbicularis oculi muscles which are supplied by the zygomatic branch of the facial nerve (7th cranial). The facial nerve emerges anterior to the mastoid and behind the earlobe. It passes through the parotid gland before crossing the condyle of the mandible then passes superficial to the zygoma and molar bone before its terminal fibers ramify in the orbicularis oculi.

Patient Selection

Indications: Regional anesthesia is suitable for elderly or medically compromised patients.

Contraindications: of regional anesthesia are the same indications of general anesthesia (see above).

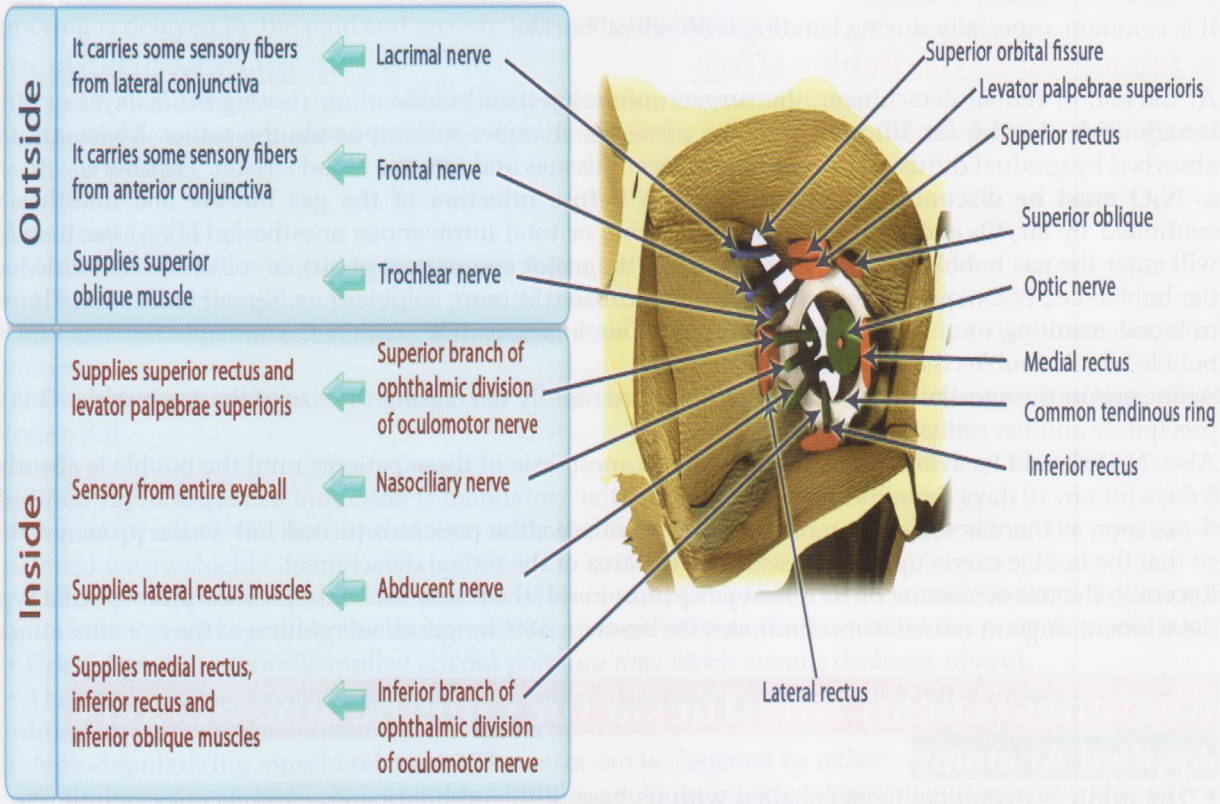


Figure 20-2: Anatomy of the orbit

Patient Preparation

1- **A preoperative visit** is important for establishment of friendly rapport with the patient.

2- **Preoperative examination (and recording)** is essential for:

- **The axial length** of the eyeball by **ultrasound scan**. Normally it is 20-24 mm. In highly myopic patients, there is an increase in axial length > 26 mm which increases the risk of global perforation and thus they should be treated with caution.
- **Extra-ocular muscles and facial nerve** because local anesthesia is avoided in patients with myopathies or Bell's palsy.

3- **The consent** is essential as usual.

4- **I.v. access** should be secured.

5- **Full cardio-pulmonary resuscitation** equipment should be available.

6- **I.v. sedation** such as midazolam 1-3 mg and/or fentanyl 12.5-25 µg is a common regimen. Avoid over-sedation because:
- It may make the patient asleep during surgery and then may wake up suddenly and in confusion trying to sit up.
- It increases the risk of apnea (see later).

7- **Instill topical local anesthetic drops** to anesthetize the conjunctiva and decrease initial stinging.

8- **Sterilization** is essential.

Monitoring

Standard monitors are required.

Presence of an Anesthesiologist

Presence of an anesthesiologist is very important to:

- monitor the patient (i.e., **Monitor Anesthesia Care, "MAC"**).
- treat complications.
- provide sedation when necessary.
- induce general anesthesia at any time if needed.

In 2001, the Royal College of Anesthetists and the College of Ophthalmologists made the following guidelines:

- Surgeons may administer topical, subconjunctival infiltration, and sub-Tenon anesthesia without an anesthetist.
- An anesthetist must be available when surgery is performed under retro- or peri-bulbar block.
- An anesthetist must be present and have sole responsibility for a list in which sedation is used.

Types of Regional Ophthalmic Anesthesia

They include:

1) Topical anesthesia (without any needle penetration).
2) Subconjunctival infiltration anesthesia.
3) Intracameral injection.
4) Sub-Tenon block (is a cannula-based block while others are considered needle-based blocks).
5) Extraconal or periconal (peribulbar) block.
6) Intraconal (retrobulbar) block.

Topical Anesthesia

Indications:

- It is used for anterior chamber (e.g., cataract) and glaucoma surgeries.
- It can be used to anesthetize conjunctiva before pre-conjunctival injections are made for other blocks.
- Patients should be mature, cooperative, can constrain eye movement, focus on bright light, resist lid squeezing, and remain relatively still.

Agent Used:

All agents are prepared as eye drops such as:

- Oxybuprocaine 0.4% (*Benoxinate*).
- Procaine (other name proxymetacaine chlorhydrate) 0.5%
- Tetracaine 1%.
- Amethocaine 1%.
- Bupivacaine 0.75%.

Both amethocaine and bupivacaine may cause stinging and cloudness of the cornea.
0.3% Na hyaluronidase is added to the local anesthesia (see later).

Technique: (without any needle break)

- Bactericidal eye drops should be administered at first to be followed by local anesthetics. Local anesthetics are applied as either:

a- **Local anesthetic solution:** It is used as topical instillation drops. It can be repeated at 5-minute intervals for 5 applications.

b- **Anesthetic gel**: such as lidocaine chlorhydrate plus 2% methyl cellulose is applied with a cotton swab to the inferior and superior conjunctival sacs. Some authors have showed an increased risk of endophthalmitis with gel-based topical anesthesia because they may form a barrier to bactericidal agents. Therefore, gel should only be applied after antiseptic agents are instilled.

- The surgeon and staff will need to ensure that good communication is maintained with the patient at all times. A mild anxiolytic premedication may be useful.
- Some surgeons augment these techniques by intracameral block (see later).

Disadvantages:

Anesthesia is not as complete as with other blocks.

- It is not appropriate for posterior chamber surgery (e.g., retinal detachment repair with a buckle).
- It needs surgeons who are fast and have a gentle surgical technique that does not require akinesia of the eye.

Subconjunctival Infiltration Anesthesia

Indications, agent used, and disadvantages are the same as those of topical anesthesia.

Technique:

Subconjunctival injection is performed by the surgeon where a small volume of local anesthetic is injected near the superior limbus.

Intracameral Block

0.1-0.5 mL of preservative free lidocaine (lignocaine) 1% with 1.5% Na hyaluronidase is injected **into the anterior chamber**. It is used usually to augment other techniques, but may have adverse affects on corneal endothelium.

Sub-Tenon or Episcleral Block

This technique is gaining popularity as an alternative to retro- and peri-bulbar anesthesia due to the following **advantages**:
- It is with fewer complications due to the use of a cannula instead of a needle.
- It can be used safely in patients with extreme myopia (axial length > 26 mm), or staphylomata.
- It can be used safely in anticoagulated patients, since any bleeding point can be cauterized directly.

Technique: (It is a cannula-based block without using a needle)

- **After topical anesthesia**, the lower lid is retracted by an assistant or by a speculum. **The conjunctiva** is **lifted** along with Tenon's capsule **in the infero-nasal quadrant** with Moorfield's **forceps**. A **small incision** is then made with **blunt-tipped Westcotts spring scissors**, which are then slid underneath to create a path between the sclera and Tenon's capsule that follows the contour of the globe and extends past the equator (Tenon's capsule is white and avascular which distinguishes it from the vascular sclera).
- While the eye is still fixed with the forceps, a **special blunt 25-mm or 19-gauge curved cannula (Southampton cannula)** is inserted and threaded in the sub-Tenon's space and introduced beyond the equator where **3-5 mL of a local anesthetic** are deposited (figure 20-3). Shorter cannulas are safer than longer ones and some use ultra-short cannulas (<6 mm). Retrograde efflux of anesthetic around the cannula and out of the incision is common. Local anesthesia injected beneath Tenon's capsule diffuses into the retro-bulbar space.
- Care must be taken to dissect in the right plane. If the cannula is placed subconjunctivally, this will become very apparent on attempting to inject the solution (figure 20-4).

Complications: They are generally less than retro- or peri-bulbar block, but there are rare reports of globe perforation, conjunctival hemorrhage, cellulites, muscle trauma with resulting strabismus, or local anesthetic spread into cerebrospinal fluid.



Figure 20-3: A sub-Tenon block cannula

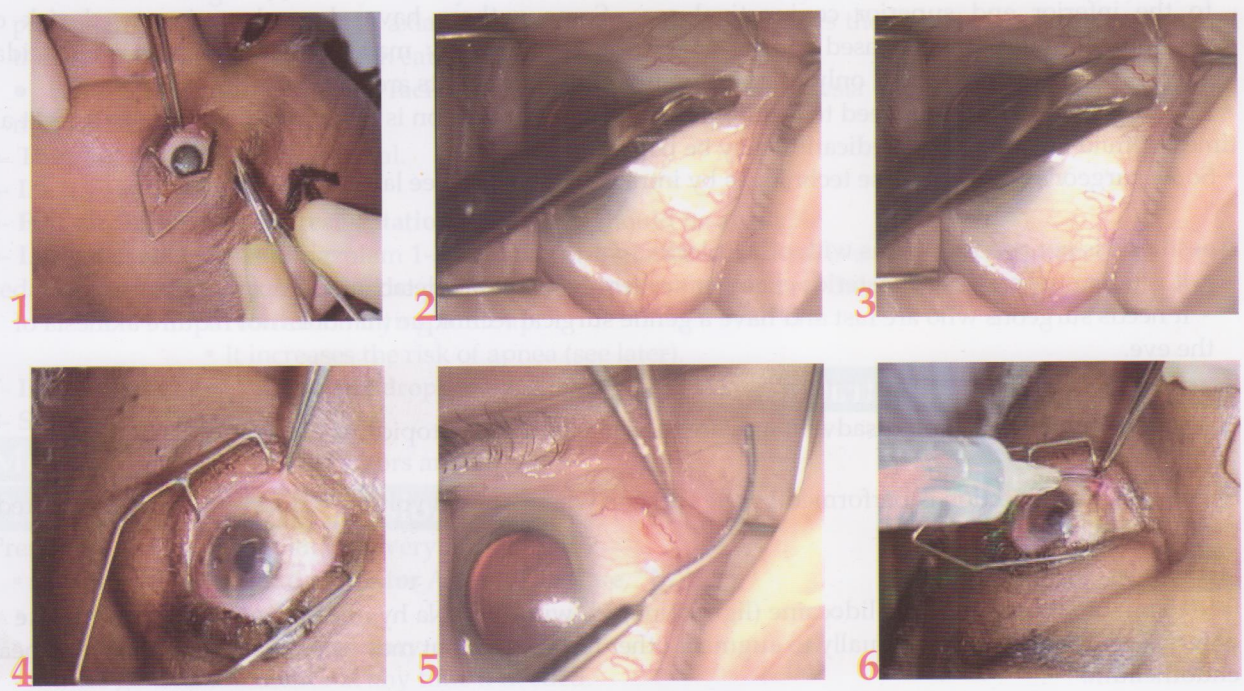


Figure 20-4: Sub-Tenon block

Extraconal or Periconal (Peribulbar) and Intraconal (Retrobulbar) Blocks

Technique:

1- Primary Gaze Position:

During performing the block, the patient should look straight ahead in the **primary gaze position** (the safest position) because:

- On looking upward or up and inward, the optic nerve is put in the path of the needle.
- On looking downward or down and outward, the optic nerve is stretched; so, it is easily punctured (figure 20-5).

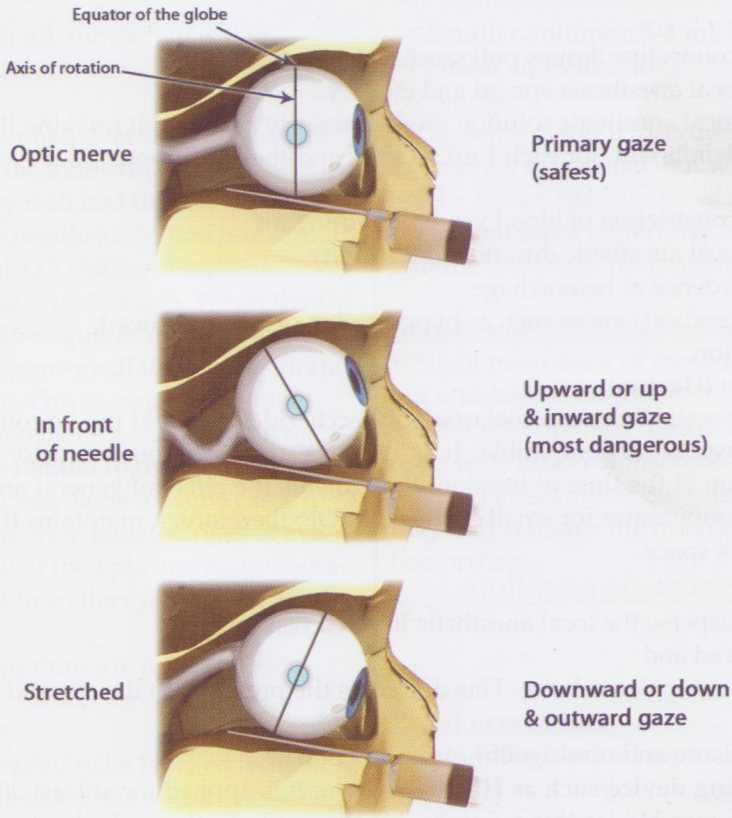


Figure 20-5: The position of the eye during regional anesthesia

2- The Needle Used:

- The best size is **25 gauge needle** because: finer needles are difficult to manipulate and larger needles cause more trauma and pain.
- The best length is **2.5 cm long needle** because: longer needles cause more trauma and pain. If longer needles are used, they should not be allowed to enter till the hub.
- **Sharp needles** are used as blunt needles cause more trauma and pain which may produce vaso-vagal syncope.
- The operator should consistently use **the same volume syringe with the same gauge** needle; so, the operator can feel the resistance to the injection and can detect easily any change in the resistance as correctly placed injections have minimal resistance.
- The operator should make sure that the hand used to hold the syringe and needle in a **pen fashion stays in firm contact with the patient's check**; therefore, any unexpected movement by the patient does not displace the needle.

3- Depth of Injection:

Injection should **not be deeper than 31 mm** from the orbital margin as this ensures that the needle will not approach the apex of the orbit as the chance of penetrating the optic nerve or damaging other important structure increases with increasing the depth of the injection. When 2.5 cm long needle is used, it can be advanced until its hub reaches the plane of the iris.

The mean distance from the temporal border of the orbital margin to the optic foramen is 50 mm.

4- Local Anesthetics Used:

• **A single agent** can be used alone effectively such as lidocaine 2%, prilocaine 2-4%, or ropivacaine 1%.

• **A combination of agents** is commonly used such as equal volumes of **bupivacaine 0.5-0.75% (especially levo-isomer) and lidocaine 2%.** Bupivacaine increases the duration of the block and provides postoperative analgesia, meanwhile lidocaine speeds the onset of the block and is less toxic. Freshly prepared preservative free anesthetic mixtures are better than the pre-prepared combinations.

• Higher concentrations are needed for the periconal block while lower concentrations are needed for the intraconal block.

5- Additives to Local Anesthetics:

a. Hyaluronidase:

Value: It hydrolyses connective tissues polysaccharides resulting in:

- improvement of local anesthesia spread and efficacy.
- *placement of the local anesthetic solution more anteriorly in the orbit (making the technique safer).*

Dose: 5 units up to 30 units/mL for each 1 mL of local anesthetic solution.

b. Epinephrine:

Value: It causes vasoconstriction of blood vessels resulting in:

- improvement of local anesthetic duration and solidity.
- decreasing the incidence of hemorrhage.

It can be omitted for medical causes such as hypertension or ischemic heart.

Dose: 1: 400 000 solution.

N.B.: Na Hyaluronate (Haelon):

It is a large molecular weight clear viscoelastic polysaccharide. It should not be confused with the enzyme hyaluronidase, the two are incompatible. It is used as a soft viscous retractor during surgery when injected by the surgeon at the time of incision. It augments the effect of general anesthesia by controlling vitreous bulge and compensates for small changes in IOP; therefore, it maintains the shape of the anterior chamber and the work space.

6- Extraocular Pressure Application:

This is important to disperse the local anesthetic injected resulting in:

- increasing its spread and
- decreasing the extra-ocular volume. This decreases the pressure on the eye and IOP.

It is done by either:

- gentle digital pressure and massage for at least 20 min or
- a **pressure-reducing device such as Honan balloon**. It is applied for at least 20 min and at a pressure of no more than 35 mm Hg (at this pressure, blood supply to the eyeball is assured) then the balloon should be removed just before the operation (figure 20-6).

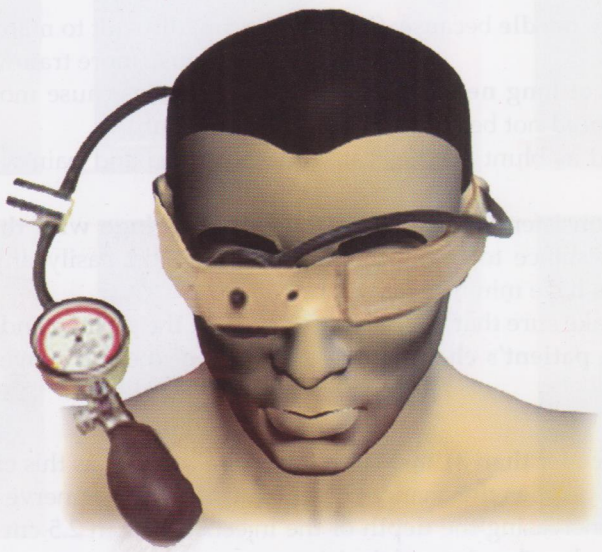


Figure 20-6: A Honan balloon

7- Techniques of Performing the Block: are either extraconal or intraconal.

A- Extraconal (Periconal or Peribulbar) Block	B- Intraconal (Retrobulbar) Block
• It involves placement of the injectate **around the cone** with diffusion of local anesthetic solution across connective tissue septa. • It is analogous to **epidural** block with **delayed onset** (the time for local anesthetic solution to diffuse via the connective tissue of the cone). • It needs: ▫ **Larger** volumes **6-8 mL** for each injection. ▫ **Higher** concentrations. Technique: • While the patient is looking straight ahead, the anesthesiologist uses his index finger to palpate the groove between the eyeball and the inferior orbital margin and insert the needle at the junction of the middle and the lateral 1/3 (**infero-temporal quadrant**) perpendicular on the skin. When **the tip of the needle passes the equator of the eyeball, it is redirected slightly supero-medially** then aspiration and injection are done. This is usually adequate. • Additional injection may be needed where the needle is inserted just **medial to the medial canthus**. This site may be sufficient alone in some cases to produce a block to the eye where the risks of eye perforation and injury of the optic nerve are less as the globe is separated from the eye by the medial rectus muscle. • Other additional injections are rarely needed (figure 20-7). **Facial nerve block:** **Facial nerve is not needed** to be blocked as its fibers are blocked during spread of the anesthetics superficially while they enter the orbicularis oculi muscle. **Complications:** Fewer complications are produced.	• It involves placement of the injectate **in the fatty compartments inside the cone** which surrounds the optic nerve. • It is analogous to **subarachnoid** block with **rapid onset.** • It needs: ▫ **Smaller** volumes: **3-4 mL** for each injection. ▫ **Lower** concentrations. Technique: • The same point of insertion as **infero-temporal** injection of extraconal, but when the tip of the needle passes the equator of the eye, **it is redirected more superiorly and medially** to float into the cone with minimal resistance. **In both extraconal and intraconal blocks:** • Slight movement of the needle to ensure that it is not attached to the globe. • After injection, the needle is withdrawn in the reverse direction of insertion. • Avoid injections at the supero-nasal quadrant as they may damage the trochlear apparatus or cause hemorrhage. **Facial nerve block:** It **should be blocked** separately (see below). **Complications:** More complications are produced.

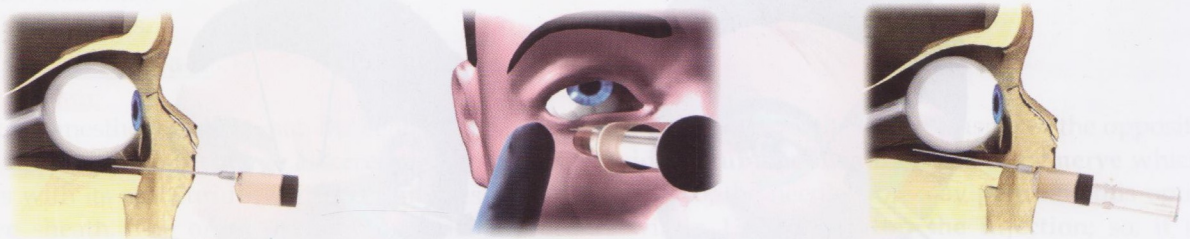


Figure 20-7: Eye block

In practice, the differentiation between retrobulbar and peribulbar is more semantic than actual. If the onset of anesthesia is rapid with a peribulbar anesthetic then mostly it has found a direct pathway or it has been injected directly into the cone (intraconal block).

Facial Nerve Block:

Value: It weakens the orbicularis oculi muscle to avoid the squeezing action of the eyelids and allow placement of a lid speculum. It is indicated only in intraconal block.

Techniques: There are different techniques.

1- **O'Brien Technique:** is the simplest method.

• The most prominent part of the zygoma, midway between the tragus of the ear and the lateral orbital margin, is used as a landmark where a 25-gauge 30 mm needle is inserted perpendicularly down to the zygoma. The needle is then withdrawn from the periosteum and aspiration is done. Then 3-6 mL are injected lateral to the lateral orbital margin.

• Gentle massage should be applied to the wheal to spread the local anesthetics and to ensure that no bleeding occurs.

2- **Atkinson Technique**: The local anesthetic is injected subcutaneously across the zygoma.

3- **Van lint Technique**: The local anesthetic is injected subcutaneously into the region of the outer canthus and directed toward the patient's eyebrow.

4- **Nadbath Technique:** It blocks the facial nerve as it exits the stylomastoid foramen under the external auditory canal in close proximity to the vagus and glosso-pharyngeal nerves; therefore, this technique is not recommended because it may cause vocal cord paralysis, laryngospasm, dysphagia and respiratory distress (figure 20-8).

5- Some authors recommend injection of 1-3 mL of local anesthetic just **under the orbicularis oculi muscle** to block the terminal fibers of the facial nerve to enhance facial nerve block.

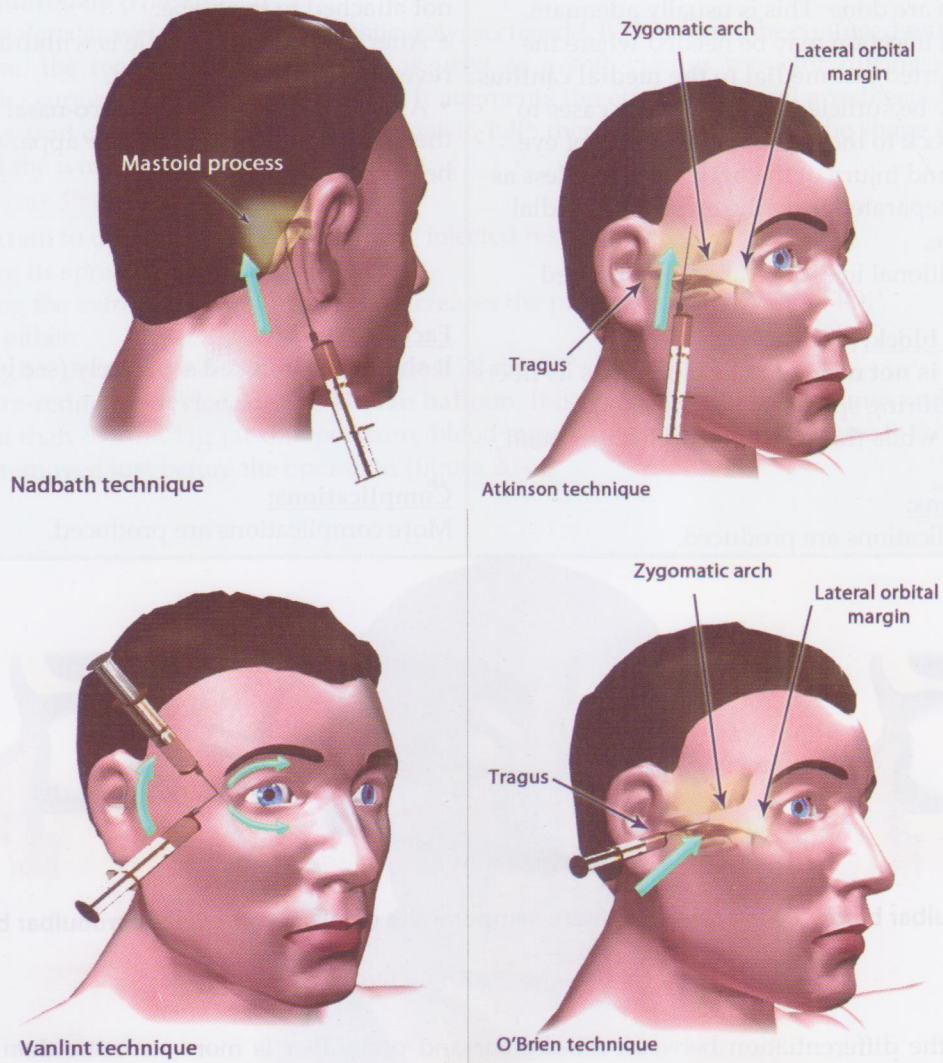


Figure 20-8: Facial nerve block

Successful Intraconal or Extraconal Blocks: are indicated by

- Anesthesia of the eye.
- Akinesia of the eye.
- Abolishment of the oculo-cephalic reflex (i.e., blocked eye does not move during head-turning).

Complications

1. Hemorrhage:

Incidence: 0.1 – 3% especially in patients with vascular disease.

Clinical Picture: It is either concealed or revealed.

a. **Venous hemorrhage:** It appears as marked blood stained ecchymosis. Extravasation of blood into the peri-orbital tissues occurs causing a mild increase in IOP.

b. **Arterial hemorrhage:** It is more serious. Extravasation of blood into the peri-orbital tissues occurs causing a marked increase in IOP.

Prevention:

1- Preoperative **control of hypertension**.

2- **Avoid:**

- **Multiple injections** as the fewer the injections into the orbit, the less the damage to the blood vessels.
- **Cutting and slicing movements** at the needle tip.
- **Thicker needles.**
- **Deep** intra-orbital injections.

3- Recommendations:

- The **infero-temporal quadrant** is the best for injection because it has fewer blood vessels and is less hazardous.
- A technique of producing **a liquid stilette of local anesthetics** in front of the advancing needle by slow injection is recommended.
- **Adrenaline** is suggested by some authors as it decreases the incidence of hemorrhage.
- **Firm digital pressure,** applied to the orbit as soon as the needle is withdrawn after intra-orbital injections, is important.
- **Blunt** Atkinson-type needles can be used, but are painful to be inserted. They may cause **vaso-vagal syncope** and can still damage blood vessels.

Treatment: is mainly directed to decrease IOP.

a. **Venous Hemorrhage:**

- Digital massage.
- Cautious application of IOP-reducing devices.

Before the decision is made to proceed with surgery or postpone it for a few days, it is advisable to measure and record the IOP.

b. **Arterial Hemorrhage:**

- Firm digital pressure usually stops the bleeding.
- Lateral canthotomy.
- I.v. acetazolamide.
- I.v. mannitol.
- Paracentesis.

2. Central Spread:

Mechanism:

a. Local anesthetics may reach the central nervous system (and/or cross the optic chiasma to the opposite eye) **around the optic nerve as cerebral dura mater provides a tubular sheath for the optic nerve** which fuses with its epineurium and is continuous with the sclera; so, the needle's tip may perforate this optic nerve sheath. The onset of symptoms usually occurs within **15-20 min after the injection;** so, it is advisable not to cover the patient's face on the operating table during this period.

b. Rarely, local anesthetics may reach the central nervous system in **a retrograde fashion up the orbital artery**, when it is cannulated by the needle's tip. The onset of symptoms, especially convulsions, usually occurs **instantaneously** and tends to resolve quickly. Orbital hemorrhage is also common.

Clinical Pictures:

Clinical pictures are variable depending upon which part of central nervous system is affected by the local anesthetics. **The midbrain** is the usual affected area due to its anatomical proximity to the optic nerve resulting in:

1- Loss of consciousness.
2- Cardiovascular instability up to cardiac arrest.
3- Respiratory depression up to respiratory **arrest** (i.e., **post-retrobulbar apnea syndrome** which occurs within 15-20 min and resolves within 1- 1.5 hours).
4- Temperature regulation disturbances.
5- Vomiting.
6- Temporary hemiplegia.
7- Aphasia.
8- Generalized convulsions.
9- Extraocular muscle palsy in the opposite eye due to affection of the contra-lateral occulomotor and trochlear nerves with loss of vision (amaurosis). This is pathognomonic of central nervous spread.

Prevention:

1- Patients should look straight ahead in the **primary gaze** position as the optic nerve is slack and out of the way of the advancing needle. If the needle touches the optic nerve, it will push the optic nerve aside due to its slackness.
2- **Avoid deep** intra-orbital injections as the optic nerve is tethered to its sheath when it merges through the optic foramen.
3- **Withdrawal of the needle 1 mm** from its maximum depth **before injection** is recommended.

Treatment: is symptomatic throughout the duration of local anesthetic action which is usually 1-1.5 hours by: 1- Intensive monitoring.
2- Cardiopulmonary resuscitation by adrenaline and mechanical ventilation.
3- Thiopentone to control convulsions.
4- When the patient is stable, continue surgery with general anesthesia.

3. Puncture of the Eyeball:

It is very rare as **the sclera is a tough structure** and in most cases is **not perforated easily.**

Risk factors:
- High myopia with axial length > 26 mm.
- Previous retinal hemorrhage.
- Posterior staphyloma.
- Deep sunken eyes with a narrow orbit.
- History of scleral buckle surgery.

Treatment:

- Global puncture is often a **double puncture of the posterior segment** of the eyeball where the tip of the needle is in the cone at the time of injection. It leads to a **good block**, but the puncture is usually recognized at the time of surgery by the **softness of the eye**.
- **In cataract surgeries**, if the block is good, the surgeon should be encouraged to proceed with lensectomy, but to stitch up the eye with twice as many sutures as normal.
- Without lensectomy, damage in the posterior segment may not be observed and a **band of scar tissue** will occur at the site of the needle track. **If it is not excised**, it may **contract and detach the retina resulting in sudden blindness.**

4. Optic Nerve Damage:

It is rare, **due to obstruction of the central retinal artery,** as injury of the artery causes a **hematoma** within the optic nerve sheath. This causes **compression and obstruction of blood flow** needing immediate surgical decompression once diagnosed.

N.B.: Central retinal artery is the first and smallest branch of the ophthalmic artery. It passes first below the optic nerve within the dural sheath of the optic nerve and then at 35 mm from the orbital margin it pierces the nerve and runs in its center to the retina.

5. Myopathy of Extraocular Muscles:

It occurs due to inadvertent injection of local anesthetic into the extraocular muscles. It causes prolonged weakness of the muscles.

6. Vasovagal Syncope:

It is common especially: in young and anxious patients.
with blunt Atkinson needle, due to painful insertion.

Treatment:
- O_2.
- Anticholinergics.
- Head-down position.

- It should be differentiated from central spread by testing the vision and extraocular mucsles in the opposite eye.

7- Oculo-cardiac reflex:

It occurs due to pressure on the eye globe by the local anesthetics.

Extra-Ocular Surgery

I) Squint (Strabismus) Surgery

Anesthetic Problems:

1- There is an increased incidence of:

- **Oculo-cardiac reflex**.
- **Malignant hyperthermia**.
- **External ophthalmoplegia syndrome**:
  - Squint and ptosis may be the presenting signs of this syndrome.
  - There is **marked cardiac and respiratory decompensation.**

  Therefore, preoperative pulmonary function tests and cardiac investigations are advisable.

2- **Avoid drugs with prolonged action on the muscle tone** as postoperative adjustable sutures may be planned.

Ketamine is preferred in children as **it does not decrease the muscle tone;** so, it allows the surgeon to test muscle power intraoperatively.

3- **There is an increased incidence of postoperative nausea and vomiting;** so, prophylactic antiemetics are essential. Postoperative nausea and vomiting represent 40-85% in children after strabismus surgery.

General anesthesia is usually done by any anesthetic technique.

II) Examination under Anesthesia

Anesthetic Problems:

1- Mainly in **children.**

2- **Day case** anesthesia.

3- Repeated anesthesia can be needed at fairly short interval.

Anesthetic Management:

It is either by:

- **Inhalational anesthesia** by a face mask which is often satisfactory.

or • **Ketamine** which is a very good agent for small children as it rarely affects airway patency, but premedications as atropine should be given to decrease the risk of secretions which may provoke laryngeal spasm. Also, it increases IOP; so, it may interfere with IOP measurement resulting in a false increase in reading.

General anesthesia **with intubation or laryngeal mask** is rarely needed.

III) Dacro-Cysto Rhinostomy

Anesthetic Problems:

Hemorrhage is the main problem which obscures the operative field; so,

- **Prepare the nose** with cocaine paste or other vasoconstrictor.
- **Adrenaline infiltration** to the operative site (by surgeon) is needed.
- **Throat pack** is mandatory as blood trickles into the nasopharynx.
- **Hypotensive anesthesia** may be needed.

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GASTROINTESTINAL DISEASES

21

• Esophageal surgery • Intestinal obstruction • Ileus	• Gastrointestinal (GI) bleeding • Acute abdomen

Esophageal Surgery

- Simple endoscopy.
- Esophageal dilatation.
- Cervical or distal esophagomyotomy (open or thoracoscopic).
- Blunt esophagectomy (esophageal resections).
- Block esophagectomy with: ▫ the stomach pulled-up into the neck.
  or ▫ colonic interposition (replaced by the colon).
- Anti-reflux operations.
- Repair of hiatus hernia.

Anesthetic Management:

Preoperative Management:

1- Preoperative Assessment of the Esophageal Lesion: Such as esophageal tumors, gastro-esophageal reflux, or systemic sclerosis (scleroderma).

- Dysphagia (is the classic symptom of all esophageal disorders), coughing and/or wheezing on lying flat.
- Heartburn, regurgitation, and aspiration resulting in **recurrent chest infection**. Chronic aspiration may cause pulmonary fibrosis and dyspnea on exertion due to:
  - ▫ Esophageal obstruction.
  - ▫ Motility disorders (achalasia) which cause esophageal dilatation, and retained collections of large volumes of undigested food within the esophagus.
  - ▫ Abnormal sphincter function.
- Anemia, weight loss, and cachexia (especially in esophageal carcinoma).

2- Preoperative Assessment of Other Systems:

- Smoking increases the risk of presence of cancer esophagus, chronic obstructive pulmonary disease, and coronary artery disease.
- Scleroderma may also affect the kidney, heart, and lung.

Esophageal Carcinoma

It represents 7% of all gastrointestinal malignancies.

Risk Factors of Esophageal Carcinoma:

- Age: Esophageal cancer increases with age.
- Sex: Males are more susceptible than females by a ratio of 7: 1.
- Race: Adenocarcinoma (50% of all esophageal cancers) is more frequent in Caucasians and Westerns, while squamous cell carcinoma is more frequent in Africans and Asians (especially china and north Iran).
- Alcohol and cigarette smoking have a synergistic effect.
- Chronic inflammation and stasis: for example caustic stricture and achalasia.
- Obesity due to increased gastro-esophageal reflux disease.
- Deficiencies of vitamins A and C and trace elements as in low socio-economic classes.

Preoperative Predictors of Postoperative Complications:

- Preoperative pulmonary dysfunction.
- History of smoking.
- Advanced age.

- Liver impairment.
- Renal impairment.
- Poor physiological and performance status as in those with ischemic heart disease, anemia, or polycythemia.
- Nutritional deficiencies.
- Diabetes mellitus.
- Preoperative chemo-radiotherapy especially in doses affecting the lung function.

These predictors should be assessed preoperatively as they are associated with increased morbidity and mortality.

Preoperative Scoring System

There are many scores, which aim to classify patients according to the risk. The most important score is

Bartel's Scoring System (1992)

Degree of Severity (Weighting)	Finding	Value (degree of severity x weighting)
Pulmonary Function (2) 1 = normal 2 = compromised 3 = severely impaired	▫ Vital capacity > 90% and PaO_2 > 70 mm Hg ▫ Vital capacity < 90% or PaO_2 < 70 mm Hg ▫ Vital capacity < 90% and PaO_2 < 70 mm Hg	2 4 6
Hepatic Function (2) 1 = normal 2 = compromised 3 = severely impaired	▫ Aminopyrine breath test > 0.4 (2.4%) ▫ Aminopyrine breath test < 0.4, no cirrhosis ▫ Cirrhosis	2 4 6
Cardiac Function (3) by cardiology opinion 1 = normal 2 = compromised 3 = severely impaired	▫ Normal risk for major surgical procedure ▫ Intermediate risk for major surgical procedure ▫ High risk for major surgical procedure	3 6 9
General Status (4) 1 = normal 2 = compromised 3 = severely impaired	▫ Karnofsky index > 80% and good cooperation ▫ Karnofsky index < 80% or poor cooperation ▫ Karnofsky index < 80% and poor cooperation	4 8 12
		Total value

The weighting is in brackets after each function. Thus if a patient has severely impaired hepatic function, this scores as a severity of 3, multiplied by the weighting for hepatic function which is 2; thus hepatic function in that patient scores 6 (the sum in the value column).

According to the total value obtained by Bartel's scores, the patients are classified into 3 groups:

Low risk group (11-15 points): 3.6% 30-day mortality.
Medium risk group (16-21 points): 8.7% 30-day mortality.
High risk group (22-33 points): 28% 30-day mortality.

N.B.: General status is assessed by using **Karnofsky Performance Scale Index**

- Able to carry on normal activity and to work; no special care needed
  100%: normal and with no complaints; no evidence of disease.
  90%: able to carry on normal activity; minor signs or symptoms of diseases.
  80%: normal activity with effort; some signs or symptoms of disease
- Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.
  70%: cares for self, but is unable to carry on normal activity or to do active work.
  60%: requires occasional assistance, but is able to care for most of his/her personal needs.
  50%: requires considerable assistance and frequent medical care.
- Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.
  40%: disabled; requires special care and assistance.
  30%: severely disabled; hospital admission is indicated although death is not imminent.
  20%: very sick; hospital admission necessary; active supportive treatment necessary.
  10%: moribund; fatal processes progressing rapidly.
  0%: dead.

Other Scoring Systems: include

1- Furguson and Durkin (2000)

It is a scoring system to predict pulmonary complications after esophagectomy for cancer.

2- POSSUM and O-POSSUM

They are discussed in chapter "the Practice Conduct of Anesthesia".

3- Preoperative Investigations:

1- **Investigations for the esophageal lesions** such as barium contrast study.

2- **Investigations for other systems** as hematology, biochemistry profile, arterial blood gases, ECG, chest x-ray, pulmonary function tests, and integrated cardio-pulmonary function capacity such as cardiopulmonary exercise testing (discussed in chapter "Cardiovascular Disease").

4- Preoperative Patient Preparation:

1- Measures **against aspiration** such as
- preoperative awake nasogastric suction.
- Antacids, H_2 blockers, metoclopramide, or omeprazole.

2- Treatment of **chest infections** (if present).

3- Correction of **anemia** and/or enteral or parenteral **nutrition.**

4- Measures against **blood loss** such as:
- Large bore i.v. catheters.
- Preparation of blood transfusion.

Intraoperative Management:

Monitoring:

Besides the standard monitors,
- Invasive blood pressure: is done in patients when a great blood loss is expected.
- Central venous pressure: also is indicated in patients when a great blood loss is expected.
- Pulmonary artery catheter: is done in patients with cardiac problems and monitors O_2 delivery.

N.B.: Patients with O_2 delivery lower than 445 mL/min/m^2 are subjected to increased mortality and morbidity even as increased anastomotic leak and pneumonia. Therefore, O_2 delivery monitoring is essential. Dopexamine infusion can increase O_2 delivery to be greater than 600 mL/min/m^2. This decreases mortality and morbidity. Dopexamine is superior than and has more advantages than adrenaline and dobutamine because it produces less ischemia than others due to:

- Dopexamine predominantly acts at the vasodilatory β_2 adrenoceptors and dopamine (DA_1) receptors; so, the increase in cardiac output is achieved mainly by increasing heart rate and increasing stroke volume without greatly increasing stroke work and O_2 demand, but still tachycardia is a disadvantage.
- Dopexamine also has some anti-inflammatory properties and may modulate the systemic inflammatory response syndrome (SIRS).

Choice of Anesthesia

a- General Anesthesia:

Induction:
- **Rapid sequence induction** with cricoid pressure in the semi-upright position.
- **Awake fiberoptic intubation** is indicated in patients with systemic sclerosis when difficult laryngoscopy is suspected.
- **Double lumen tube** (usually a left tube such as left Robertshaw tube) is used for procedures involving thoracoscopy or right thoracotomy, which are indicated for lesions in the upper 1/3 of the esophagus.

Maintenance:

The choice of anesthesia depends on the patient's hemodynamics and associated diseases.

b- Thoracic Epidural Anesthesia:

It can be used alone or combined with general anesthesia. Epidural anesthesia can be accomplished with local anesthetics alone or opioids alone or both. In most centers, it is routinely performed with esophagectomy.

Advantages:
- Thoracic epidural anesthesia decreases mortality and morbidity.
- Thoracic epidural analgesia with local anesthetics can block the cardiac sympathetic innervations, which comes from T_1-T_5. Sympathetic blockade will reduce myocardial O_2 demand and coronary

vasoconstriction and thus may reduce adverse cardiac events (myocardial ischemia) intraoperatively and postoperatively for the first 24 hours.

- The vasodilator effects of epidural anesthesia can reduce the incidence of postoperative heart failure in high-risk surgical patients.
- The sympathetic blockade by epidural anesthesia can modify the postoperative hypercoagulability state and may decrease the risk of venous thromboembolism.
- Epidural anesthesia reduces postoperative ileus.

Intraoperative Problems:

1- The anesthesiologist may be asked to pass **a large diameter bougie** into the esophagus as a part of the surgical procedure. Great caution must be taken to avoid **pharyngeal or esophageal injury.**

2- **Great blood loss** especially in:

- Trans-hiatal (blunt) esophagectomy via an upper abdominal incision and left cervical incision.
- En block thoracic esophagectomy via posterior thoracotomy, a large abdominal incision and left cervical incision.
- Colonic interposition.

3- **Intraoperative hypothermia** due to increased blood loss and lengthy surgery; therefore, fluid warmer, forced air body warmer…etc are indicated.

4- **During the trans-hiatal approach:**

- Substernal and diaphragmatic retractors can interfere with superior vena cava and with cardiac function.
- The esophagus is freed up blindly from the posterior mediastinum by blunt dissection. The surgeon's hand transiently ▫ interferes with cardiac filling producing **profound hypotension.**
  ▫ produces marked vagal stimulation causing **severe bradycardia.**

5- During colonic interposition, avoid graft ischemia by preventing hypoxia, metabolic acidosis, hypotension, and low hemoglobin concentration.

Extubation:

Awake extubation is usually indicated as follows:

For minor procedures, it is done in the operating room.
For major procedures, it is done in the intensive care unit.

Postoperative Management and Intensive Care Considerations:

Patients are managed in the intensive care unit for major procedures.

1- Postoperative Ventilation: is usually indicated for major procedures e.g., esophagectomy.

2- Postoperative Analgesia: is usually performed by thoracic epidural analgesia.

3- Postoperative Complications:

- Pulmonary complications such as **acute lung injury** which occurs in 50% of patients following esophagectomy. It may progress to **respiratory failure** or **acute respiratory distress syndrome**.

Causes of postoperative acute lung injury or acute respiratory distress syndrome:

- ▫ Surgery causes direct trauma to intrathoracic structures including the lungs and lymphatic drainage, or thoracic duct.
- ▫ During one-lung ventilation, the ventilated lung is often subjected to hyperoxia to compensate for intra-pulmonary shunting, high inflation pressures and volume trauma; all of which may contribute to lung damage.
- ▫ The non-ventilated lung is susceptible to ischemia/reperfusion injury with the consequent release of pro-inflammatory mediators.
- ▫ Postoperatively, patients are at risk for overspill and soiling of the lung with gastric contents.

- Injury to the phrenic, vagus, or left recurrent laryngeal nerve.
- Disruption of the anastomosis occurs in 5-10% causing severe mediastinitis (it results in greenish or yellowish discoloration of the fluid in the chest drains). It is associated with high mortality rates.

Achalasia

It is characterized by motor disorder of the distal 2/3 of the esophagus, failure of relaxation, dysphagia, and regurgitation, risk of malignant change, increased risk of gastric reflux.

Intestinal Obstruction

Intestinal obstruction can occur in either small or large intestine. Intestinal obstruction is either:

- **Functional obstruction (paralytic, adynamic, or inhibition ileus)** or
- **Mechanical obstruction** due to presence of an actual physical barrier that interferes with the normal progression of intestinal contents. Mechanical obstruction is divided into:
  - **Simple obstruction:** involves only the bowel lumen while the blood supply remains normal.
  - **Strangulated obstruction**: impairs blood supply and lead to necrosis of the intestinal wall.

N.B.: **A closed-loop obstruction** occurs when the bowel lumen is occluded in two or more locations. It is often associated with strangulation because blood supply may be compromised even before clinical evidence of intestinal obstruction exists.

Causes of Intestinal Obstruction:

A) Small Intestinal Obstruction: represents 60-80% of bowel obstruction.

1- **Postoperative adhesions** from previous abdominal surgery are **the most common cause** (75% of cases). It has insidious onset.
2- **External hernias** through the abdominal wall that become incarcerated are the second most common cause.
3- **Internal hernias** such as that through the obturator foramen or through the diaphragm.
4- **Neoplasms** within or extrinsic to the small bowel may produce obstruction directly or by mass effect.
5- **Volvulus or intussusception** is associated with abrupt onset.
6- Other less common causes include:
- Gallstone ileus.
- Ingested foreign bodies.
- Inflammatory fibrosis.
- Crohn's diseases.
- Posttraumatic hematoma.

B) Large Intestinal Obstruction: represents 20-40% of bowel obstruction.

1- Carcinoma is the most common cause.
2- Diverticular disease.
3- Volvulus (figure 21-1).
4- Inflammatory disorders
5- Benign tumors.
6- Fecal impaction
7- Adhesions.
8- Intussusception.

Both adhesions and intussusception are very rare causes.

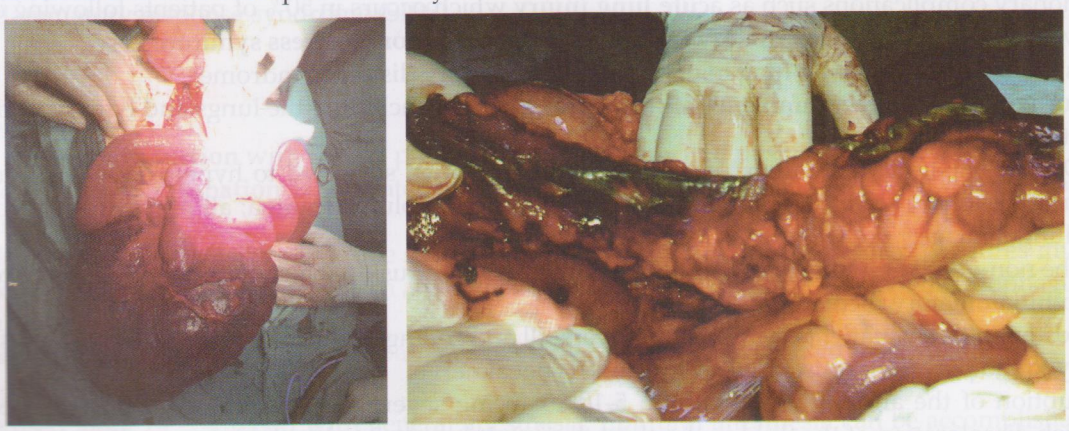


Figure 21-1: Two patients with intestinal obstruction; the left one is due to cecal volvulus with gangrenous cecum and the right one due to ulcerative colitis with ischemic perforated colon

Clinical Picture:

There are 4 cardinal signs of intestinal obstruction, which include:

1- **Acute crampy abdominal pain:**

- In small intestinal obstruction, pain is colicky and diffuse alternating with quiescent periods. The duration of the quiescent period depends on the site of intestinal obstruction:

- With high obstruction, quiescent period is about 4-5 minutes.
- With low ileal obstruction, quiescent period is about 15-20 minutes.
- With strangulation, pain is steady and severe.

• In large intestinal obstruction, pain is deep-seated cramping referred to the hypogastrium. Pain from obstruction of sigmoid colon usually radiates to the left lower quadrant.

2- **Vomiting: Reversal of peristalsis and mechanical obstruction** push the intestinal juice in addition to the gastric juice to produce a full stomach with increased intra-abdominal pressure. This increases the incidence of vomiting and regurgitation especially in higher levels of obstruction. Vomiting becomes progressively more feculent as the illness progresses.

3- **Constipation or obstipation:** especially in large bowel obstruction.

4- **Abdominal distension:** occurs due to accumulation of fluids and gases (most of them are due to swallowed air).

There are other signs that include:

- **Localized tenderness**.
- **Fever**.
- **Leukocytosis** (usually 15000-20000/μL) that indicates strangulation.
- **Rectal examination that** is usually normal in small bowel obstruction. **In large bowel obstruction, occult blood** may be present on rectal examination, which indicates carcinoma, while **fresh blood** is characteristic of diverticular disease and intussusception.

Patients are usually geriatrics with poor general condition.

Preoperative Management:

The time available for preoperative preparation and management of the patient with intestinal obstruction varies from only a few minutes to 12 hours or more. This depends on the balance between the benefits of preoperative resuscitation and those of urgency of the surgery.

1) Fluid and Electrolyte Imbalance:

a. Dehydration:

• **Normally, 7-9 liters** of fluids are secreted into the upper intestinal tract daily (including saliva 500-2000 mL, gastric juice 1000-2000 mL, bile 300-600 mL, pancreatic juice 300-800 mL, and succus entericus 2000-4000 mL) and reabsorbed so that, only 400 mL pass through the ileo-cecal valve.

• **In small intestinal obstruction**, fluid loss occurs due to:

- **accumulation of fluids** in the bowel above the obstruction,
- **increased secretion** due to prostaglandin release in response to increased intra-luminal pressure,
- **decreased reabsorption** once the intra-luminal pressure exceeds 20 cm H_2O.

This causes loss of isotonic salt (plasma-like) water resulting in isotonic contraction of extracellular volume. Therefore, dehydration and increased hematocrit occur.

• The accumulated fluid depends on the duration of obstruction as follows:

- At **early stages, 1500 mL** of fluid accumulate in the bowel.
- At **well established** cases with vomiting, **3000 mL** of fluid accumulate in the bowel.
- At **late stages** with hypotension and tachycardia, **6000 mL** of fluid accumulate in the bowel.

• The **degree of dehydration** is evaluated by **the duration of illness**, presence of **vomiting, skin elasticity, sunken eyes, oliguria, arterial blood pressure, heart rate and central venous pressure.** This is discussed in more details in the chapter of "Cardiovascular Diseases".

• The degree of extracellular fluid loss can be monitored by serial hematocrit (Hct) determinations. A rise in the Hct is proportional to the amount of fluid loss e.g., if Hct increases to 55%, this indicates that about 40% of plasma and extracellular fluid volume have been lost.

• **Treatment:**

2-6 liters of i.v. fluids are needed according to the degree of dehydration. The I.v. fluid is usually **lactated ringer,** because the fluid lost is similar to the plasma, or **normal saline**.

b. Electrolyte Disturbances:

1. Hyponatremia and Hypochloremia:

They occur because the accumulated fluid in the bowel and the vomitus contain high concentrations of Na^+ and Cl^- ions.

2. Hypokalemia: is mainly due to **renal mechanisms**:

- Secondary to metabolic alkalosis i.e., after drop of Cl^- ion concentration, there is exchange of Na^+ for K^+.
- Secondary to hyperaldosteronism due to the loss of water.

Hypokalemia should be corrected by i.v. potassium infusion.

c. Acid-Base Imbalance:

1. Metabolic Acidosis: is more common. It occurs due to:

- Dehydration and loss of alkaline intestinal secretions.
- Starvation ketosis.

It is corrected by $NaHCO_3$ as follows: half correction = 1/3 body weight x deficit/2 then according to the arterial blood gases. Actually, correction of dehydration produces spontaneous correction of metabolic acidosis.

2. Metabolic Alkalosis: is less common. It occurs due to:

- Repeated vomiting causing loss of gastric HCl which in turn leads to the loss of H^+ and Cl^- ions. This causes hypochloremic alkalosis.

Generally,

- **High small** intestinal obstruction causes **severe** dehydration, electrolyte and acid base disturb-ances.
- **Low small** intestinal obstruction causes **mild** dehydration, electrolyte and acid base disturbances due to absorption of fluid above the obstruction.
- **Large** intestinal obstruction causes **minimal** dehydration, electrolyte and acid base disturbances because fluid sequestration progresses more slowly as the large bowel is a primary storage organ with little secretory and absorptive functions.

2) Bowel and Abdominal Distention:

Bowel distention occurs due to accumulation of fluids and gases, which results in:

- **Blockade of the venous outflow:** This causes subsequent extravasation of blood and fluids into the bowel wall leading to **edema of the bowel wall**.
- **Blockade of the arterial blood supply** to the obstructed segment: This causes **strangulation and intestinal gangrene**, which increases the permeability of the bowel wall with loss of red blood cells into the bowel and peritoneal cavity (this may need to be restored by whole blood or packed red blood cells). In addition, there is a leak of toxic materials into the peritoneal cavity, which may cause **septic shock**.
- Hindering of **diaphragmatic** movement: This causes inadequate ventilation.
- Decreasing **venous return** due to:
  - Distention, which decreases the negative intra-thoracic pressure leading to a decrease in venous return.
  - Direct venocaval compression by intra-peritoneal tension, which decreases venous return.

  On surgical incision, sudden escape of fluids into the peritoneal cavity may cause severe hypotension; so, allow gradual escape of fluids and monitor blood pressure frequently during incision.
- Progressive distention may cause **rupture of the colon** (usually at the cecum) especially in the presence of a competent ileocecal valve.
- Progressive distention may cause a **tense abdominal wall**. This causes:
  - Higher incidence of reverse peristalsis.
  - More need of deeper anesthesia and muscle relaxants to provide adequate operative conditions.

Abdominal decompression should be performed preoperatively by:

a. **A Short stomach tube: (a nasogastric tube):** It is used at first to decompress and empty the stomach.
For example: - A Sump tube: is more efficient, because it is composed of a double lumen, one for aspiration and the other to allow air into the stomach.
- A Simple Levin tube: is less efficient, because it is composed of only a simple lumen.

b. **A long intestinal tube:** It is used to decompress and empty the intestine.
For example: Miller-Abbott tube: has an incorporated balloon containing mercury at its tip, which aids in its passage through the pylorus into the small bowel.

3) Respiratory Problems:

They occur due to
- abdominal distention, which **hinders the diaphragm** resulting in inadequate ventilation. This decreases tidal volume and functional residual capacity and causes a decrease in PaO_2 and an increase in $PaCO_2$.
- weakness of intercostal muscles due to **hypokalemia**.

4) Cardiovascular Problems:

a- Hypotension and Tachycardia up to shock due to:

- Hypovolemia.
- Decreased venous return.

- Septic shock, which occurs due to trans-peritoneal absorption of toxins from the gangrenous loop.
- Hyponatremia, which also causes confusion and somnolence.

b- Arrhythmias (mainly ventricular) due to hypokalemia.

5) Vomiting, Regurgitation, and Aspiration:

Higher levels of obstruction are associated with more vomiting and regurgitation.

Preoperative Investigations:

1- Plain Abdominal X-ray in Supine and Erect Positions:

They are performed to ensure the diagnosis of intestinal obstruction. It shows the following:

- **Bowel dilatation proximal** to the point of obstruction.
- **A ladder-like pattern** of dilated small bowel loops.
- **Gas-fluid levels** (gas-fluid levels can occur also in gastroenteritis, acute pancreatitis, severe constipation, and severe aerophagia) (figure 21-2).

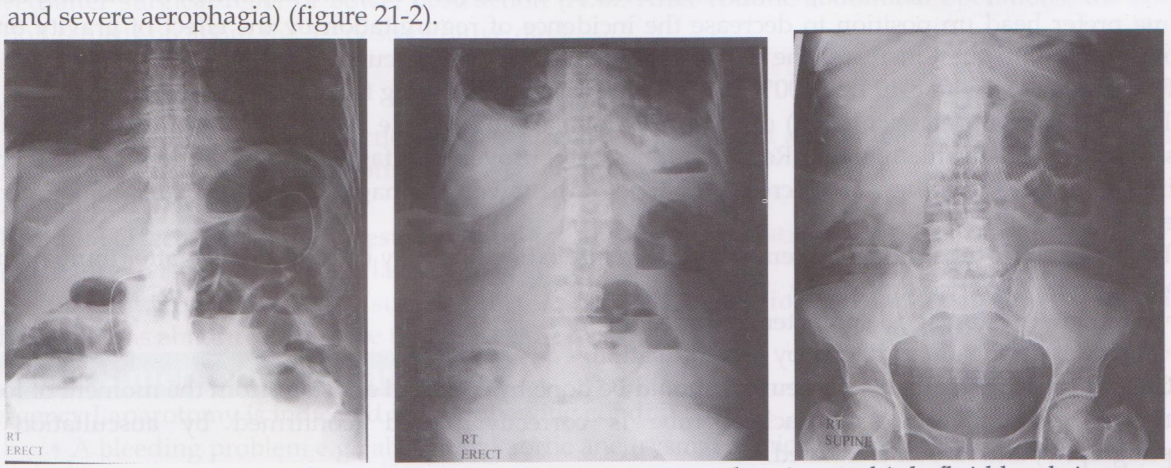


Figure 21-2: Two plain abdominal x-rays in the erect position showing multiple fluid levels in two different patients (left and middle images) and distended bowel loops in the supine position (right image)

- When strangulation and necrosis occur, loss of mucosal regularity, accumulation of gas within the bowel wall, and "thumbprinting" of the bowel wall may occur.

N.B.: Contrast studies are usually not required and should not be performed because of the risk of barium peritonitis if a perforation is present.

2- Endoscopy:

Sigmoidoscopy and colonoscopy are often beneficial in establishing the diagnosis. Care must be exercised on advancing the endoscope to prevent accidental perforation of an attenuated colonic wall. Endoscopy can be used as a therapeutic palliative procedure to create a lumen in an inoperable case.

3- Investigations to detect Complications:

- Hematocrit to detect hemoconcentration.
- Electrolytes measurements to detect hyponatremia and hypokalemia.
- Complete blood picture to detect leukocytosis.
- Arterial blood gases to detect acid-base disturbances.
- Increased serum amylase.

Premedications:

- **Avoid** all **oral** premedications.
- **Avoid** drugs that may **inhibit respiration** e.g., opioids and sedatives.
- **Avoid anticholinergics** e.g., atropine if fever or tachycardia occurs.
- **Avoid antacids or H_2 blockers** although there is a risk of aspiration because:
  - they may stimulate vomiting.
  - they are of low value if a large volume of fluids is already sequestrated in the bowel e.g., high intestinal obstruction.

Intraoperative Management:

Choice of Anesthesia:

a- Regional Anesthesia: such as subarachnoid or epidural block.

Regional anesthesia should be avoided if significant fluid depletion is suspected.

b- General Anesthesia:

Monitoring:

Besides the standard monitors, urine output, central venous pressure, and pulmonary capillary wedge pressure are beneficial.

Induction and Intubation:

Due to the increased risk of aspiration, induction and intubation can be performed as follows:

1. Awake Intubation:

It is indicated in a cooperative patient by spraying the patient's lip, tongue and pharynx with topical anesthetics. Avoid anesthesia of the larynx by superior laryngeal nerve block or trans-tracheal injection in these patients to avoid loss of protective reflexes of the larynx against vomiting or regurgitation.

2. Rapid Sequence crash Induction:

- It is done in supine or lateral position with head down tilt (10°) to avoid aspiration if vomiting occurs. Some prefer head up position to decrease the incidence of regurgitation by the effect of gravity on the stomach content, but it increases the risk of aspiration if vomiting occurs.
- Preoxygenation with 8-10 L of 100% O_2 for 3-5 min via a well-fitting facemask is essential.
- Precurarization (defasciculation) dose of non-depolarizing muscle relaxants should be given to avoid fasciculations of suxamethonium. Recently, it has been proven that fasciculations, although they increase intra-gastric pressure, they also increase the tone of the lower esophageal sphincter; thus do not increase the risk of aspiration.
- The nasogastric tube should be removed before intubation and may be reintroduced after intubation to:
  - allow effective cricoid pressure.
  - avoid lower esophageal sphincter dysfunction.
  - avoid hindering of laryngoscopy and intubation.
- **Cricoid pressure (sellick's maneuver)** should be done by a trained assistant from the moment of loss of consciousness until the endotracheal tube is correctly placed (confirmed by auscultation and capnography) and its cuff is inflated.

N.B.: Properly performed cricoid pressure provides a barrier against at least 100 cm H_2O of esophageal pressure.

- I.v. agents:
  - Thiopentone is a good choice if there is no hypotension.
  - Ketamine or etomidate are good choices if there is hypotension.

Maintenance:

- O_2, potent inhalational agent, non-depolarizing muscle relaxant, and mechanical ventilation are usually used.
- Careful titration of doses of inhalational agents is needed to avoid severe hypotension.
- **N_2O should be avoided** in bowel obstruction because it increases gas distention, which **increases intra-luminal gas volume and pressure. This results in:**
  - more increased abdominal distention.
  - increased bowel ischemia and necrosis.
  - difficulties with abdominal closure at the end of surgery.

Extubation:

- **Awake extubation** in the left lateral position is indicated after returning of upper airway reflexes and after good suction; the suction should be kept ready, then keep the patient in this position afterwards.
- There may be **a difficulty in reversing the paralysis of non-depolarizing muscle relaxants** leading to **recurarization** caused by:
  - **Relative over-dosage due to contracted extracellular volume** in these patients; this causes higher plasma level and prolonged effects.
  - **Poor peripheral blood flow and low flow states,** which result in **slowing down the onset** of paralysis and recovery and **decreasing the urine output which in turn decreases the plasma clearance**. Therefore, these drugs will exert an action after the effect of neostigmine has worn off.
  - **Hypokalemia,** which increases the sensitivity to non-depolarizing muscle relaxants.
  - **Metabolic acidosis.**
  - The use of certain **antibiotics** e.g., aminoglycosides as garamycin either parentrally or intraperitoneally.

Postoperative Management and Intensive Care Considerations:

Continue the preoperative management such as fluid and electrolyte correction, respiratory and cardiovascular monitoring.

1- Postoperative Fluid Loss and Auto-infusion:

In the **immediate postoperative period, significant fluid loss is seen mostly secondary to 3rd spacing**. This fluid loss gradually decreases over time. Usually by **about the 3rd postoperative day**, there is a reverse in direction as **fluid is transferred back into the vascular compartment i.e., auto-infusion** which may be added to the daily fluid requirements of the patient resulting in **congestive heart failure** especially if the patient is elderly with limited multi-organ reserves.

2- Postoperative Ileus:

It is common due to presence of **hyponatremia and hypokalemia**; therefore, repeated (serial) determination of serum Na^+, and K^+ should be done and managed.

3- Postoperative Abdominal Decompression:

It should be continued for **5-6 days** postoperatively because return of normal intestinal motility is usually delayed after surgical relief of bowel obstruction (N.B.: After routine abdominal operations, the bowel function returns on about the 3rd postoperative day).

4- Postoperative Respiratory Problems (especially Hypoventilation):

They may occur because:

- Although the intestinal obstruction has been relieved, significant **abdominal distention** may remain **hindering the diaphragmatic motion**.
- **Abdominal pain** is present.
- **Residual effects of inhaled anesthetics and i.v. anesthetics** are still present.
- **Difficulty to reverse muscle relaxants** may occur.
- As after any upper abdominal surgery, there is **a 15-20% reduction in functional residual capacity,** which remains abnormal for more than a week.

The sick Emergency Laparotomy

Emergency Laparotomy is indicated in the following conditions:

- A bleeding problem e.g., abdominal aortic aneurysm, splenic lacerations, or avulsed vessel.
- Intestinal perforation e.g., perforated duodenal ulcer or intestinal ischemia.
- Acute intestinal obstruction.

Ileus

Definition: It is functional failure of the normal intestinal transit.

Pathogenesis: It is poorly understood, but stimulation of the inhibitory adrenergic neurons may play an important role.

Types:

1. Adynamic, Inhibition, or Paralytic Ileus:

There is **decreased or absent motility** due to **neuromuscular inhibition** e.g., **postoperative ileus.** It is the most common type.

Causes:

1- Gastrointestinal tract surgery: Paralytic ileus occurs after every intra-abdominal operation. It affects different parts of the gastrointestinal tract differently as follows:

Normally small bowel functions recover within 1 day, gastric motility recovers within 1-2 days, and colon motility recovers within 3-5 days.

These periods are prolonged if it is associated with other factors such as opioids…etc.

2- Other conditions associated with paralytic ileus and prolong postoperative ileus:

- A ruptured viscus.
- Intraperitoneal inflammation e.g., acute appendicitis, acute pancreatitis, peritonitis
- Hematoma.
- Anoxic injury.
- Drugs e.g., opioids, anticholinergics, antacids, anticoagulants, phenothiazines, and ganglion blockers.
- Vertebral fractures or injuries of the spinal cord.
- Renal colic or uremia.
- Severe infections of either the thoracic or the abdominal cavity.
- Wound infection.
- Diabetic coma.
- Electrolyte disturbances e.g., hypokalemia, hyponatremia, and hypomagnesemia.

Clinical Picture:

- No abdominal pain is present or only mild to moderate abdominal pain, which is continuous rather than colicky.
- Discomfort of abdominal distention is usually present.
- Symptoms of the underlying conditions such as prostration from a ruptured viscus.
- Dehydration is common due to fluid translocation into distended loops of bowel.

Investigations:

- **Upright position abdominal x-ray** can differentiate between ileus and simple mechanical obstruction.

Sign	Simple Mechanical Obstruction	Adynamic Ileus
- Gas in intestine	- Large bow-shaped loops in ladder pattern	- Copious gas diffuses via the intestine
- Gas in colon	- Less than normal	- More and scattered through the colon
- Fluid level	- Definite	- Often very large throughout
- Peritoneal exudates	- None	- Absent or present with peritonitis
- Diaphragm	- Slightly elevated; free motion	- More elevated; decreased motion

N.B.: Pseudo-obstruction (Ogilvie's Syndrome) of the Colon: is severe form of paralytic ileus that often arises in bedridden patients who have serious systemic illness. Plain films show distension of the colon, which is localized to the right colon with cutoff at the splenic flexure. It requires fiberoptic colonoscope decompression.

2. Spastic Ileus:

It is uncoordinated motility due to contracted bowel musculature, which occurs with **heavy metal poisoning, porphyria and uremia.**

3. Ileus of Vascular Occlusion:

It is uncoordinated motility due to **ischemia.**

Management:

1- Treatment of the cause e.g., correction of metabolic abnormalities.
2- Nasogastric decompression or fiberoptic colonoscopic decompression.
3- I.v. hydration.
4- Nutritional support if needed.
5- Surgical treatment either enterostomy or colostomy if other measures fail.

There is no effective specific drug therapy.

Gastrointestinal (GI) Bleeding

Upper Gastrointestinal Bleeding	Lower Gastrointestinal Bleeding
Definition: Upper GI bleeding is defined by the location of bleeding lesion proximal to the ligament of Treitz (the junction between the duodenum and jejunum).	**Definition:** Lower GI bleeding is defined by the location of bleeding lesion distal to ligament of Treitz. Most often, the source of bleeding is colonic.
Incidence: • 5-6 times more common then lower GI bleeding. • Twice times more common in men than women.	**Incidence:** • Less common than upper GI bleeding.
Clinical Picture: • **Hematemesis** (vomiting of blood or via a nasogastric tube) is **the classic presentation**. It is either: ▫ **Bright red blood** which indicates recent active bleeding or ▫ **Coffee ground** which indicates older blood that has had time to be reduced by acid in the stomach. • **Melena** is black tarry stools with a foul odor caused by degradation of blood in the small intestine and colon. • **Hematochezia** is bright red blood from the rectum or maroon (brown) color stools with clots may occur with severe brisk upper GI bleeding (usually with hypertension). • Clinical picture of **hypovolemic shock** may be present. • **Blood urea nitrogen (BUN)** concentration is usually **higher than 40 mg/dL** due to the absorbed nitrogen load in small intestine.	**Clinical Picture:** • **Hematochezia** is the classic clinical presentation. • **Melena** may occur if bleeding is proximal to the cecum. • Clinical picture of **hypovolemic shock** may be present. • BUN is not significantly increased in lower GI bleeding.

Causes: **1- Mucosal erosive disease** such as **gastritis or esophagitis** due to infections as candida, cytomegalovirus; or drug-induced by aspirin, non-steroidal anti-inflammatory drugs, or tetracycline; or due to stress or alcohol use. **2- Peptic ulcer disease (duodenal or gastric)** due to infections as Helicobacter pylori infection, aspirin, non-steroidal anti-inflammatory drugs (due to prostaglandins inhibition), or stress-induced as in major trauma, burn, sepsis, or multi-organ system failure. **3- Varices and portal hypertension** (esophageal, gastric, or portal hypertensive gastropathy). **4- Vascular malformation** such as arteriovenous malformations, idiopathic angiomas, radiation-induced telangiectasia. **5- Traumatic postoperative** as Mallory-Weiss tear or foreign body. **6- Tumors:** • **Benign** as polyps. • **Malignant** as adenocarcinoma, sarcomas, cacinoid, melanoma, or Kaposi's sarcoma. **7- Miscellaneous** such as hemobilia, Meckel's diverticulum.	**Causes:** **1- Anatomic:** colonic diverticulosis. **2- Inflammatory** such as ischemic colitis, infectious colitis, inflammatory bowel disease, or radiation colitis. **3- Vascular mal-formations** such as arteriovenous malformations as idiopathic angiomas or radiation-induced telangiectasia. **4- Tumors:** • **Benign** as polyps. • **Malignant** as carcinoma. 5- Others such as hemorrhoids, ulcer or fissure, post-biopsy, or post-polypectomy.
Management: **1- ABCDE resuscitation;** "A" airway, "B" breathing, "C" circulation, "D" disability, or "E" exposure. **2- Esophago-duodenoscopy or arteriography** is used as a diagnostic and therapeutic tool. Diagnostic: Endoscopy can diagnose the cause of the bleeding e.g., duodenal ulcer, gastric ulcer, or erosive gastritis. **Recently, capsule endoscopy** is used where a small camera/capsule is swallowed by the patient and transmits 360-degree pictures throughout the upper GI tract. Another new endoscopic technique is **double-balloon enteroscopy**, which allows for endoscopic examination of the entire small bowel. Therapeutic: **a- Peptic ulcer:** • **Injection therapy** with a needle with retractable tip, with either vasopressin or terlipressin: ▫ **Vasopressin** is given as either localized infusion, 20 units over 20 min, then 0.4 unit/min by selective arteriography or i.v. infusion 0.4-0.8 unit/min, but may produce myocardial ischemia or congestive heart failure. ▫ **Terlipressin** is given as 2 mg i.v. followed by 1-2 mg i.v. 4-6 hourly until bleeding is controlled for up to 72 hours. • Use of **a bipolar coagulation or heater probe** to coagulate the site of bleeding vessels. • **Endoscopic clip application**. **b- Varices:** • **Endoscopic sclerotherapy** with a sclerosant (routinely **5% ethanolamine**) injected via a retractable-tip needle into the varix and/or surrounding tissues, leading to coagulation necrosis and variceal thrombosis. Sclerotherapy may produce complications such as esophageal perforation, pleural effusion, esophageal stricture, or ulceration. • **Endoscopic band ligation** with a rubber band. **3- Pharmacological therapy:** **a- Peptic ulcer: Proton pump inhibitors** are used to produce acid suppression where clot lysis and platelet inhibition occurs at pH less than 6. **b- Varices:** • **Octreotide**; a long-acting analogue of somatostatin is used as it decreases splanchnic blood flow. It is given as a bolus 50 µg followed by infusion 50 µg/hour for 3-5 days postoperatively. • **I.v. propranolol** (Nonselective β-blocker) and **i.v. nitroglycerin** are used to decrease the portal pressure. **4- Balloon tamponade:** There are many types such as Sengstaken-Blakemore, Minnesota, or Linton tubes (figure 21-3). A **Sengstaken-Blakemore tube** is a large-bore rubber tube, usually containing two balloons (esophageal and gastric) and two further lumens (esophageal and gastric) that open above and below the balloons. It is used to manage esophageal variceal bleeding after failure of endoscopic and pharmacological therapy. After application and inflation of gastric balloon (usually enough), traction is performed to compress varices for 12-24 hours up to 3 days. **5- Surgical treatment:** is indicated in severe and recurrent bleeding.	**Management:** **1- ABCDE resuscitation;** "A" airway, "B" breathing, "C" circulation, "D" disability, or "E" exposure. **2- Colonoscopy (sigmoidoscopy or anoscopy)** is used as a diagnostic and therapeutic tool where **localized vasopressin injection, bipolar coagulation, sclerotherapy, and endoscopic clips** can be applied. **3- Radionuclide imaging** to diagnose the bleeding site can be used where radiolabeled red blood cells are injected intravenously, and focal collections of radiolabeled material are detected by scintigraphy. **4- Angiography is also used with technetium-99** to detect the site of bleeding. **5- Surgical treatment:** is indicated in severe and recurrent bleeding.

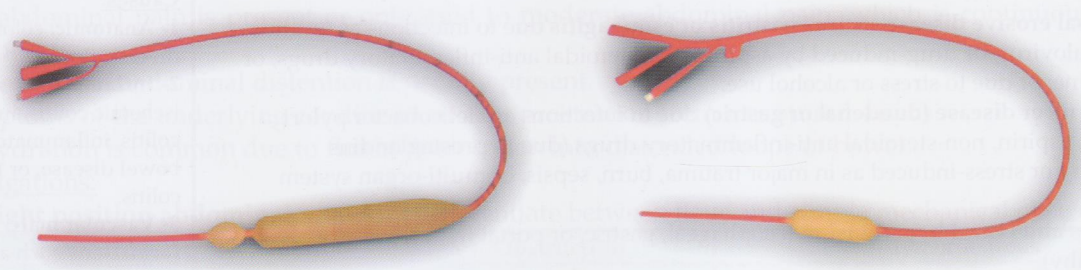


Figure 21-3: A Sengstaken-Blakemore (left) and Linton tube (right)

Acute Abdomen

Types: Abdominal pain can be divided into three categories:

a- Visceral Pain:

- It is transmitted through the **autonomic nervous system** through **C fibers** located intramurally in hollow viscera and in the capsule of abdominal organs.
- It is caused by stretching and distension that result in increased wall tension, inflammation, ischemia, torsion, compression, and increased certain chemicals.
- Pain is **dull, crampy, or aching** in nature.

b- Somatic Pain:

- It is transmitted through **A-δ fibers** of spinal nerves.
- It is caused by irritation of the parietal peritoneum and arises as a response to acute changes in pH or temperature, as seen with bacterial or chemical inflammation.
- Pain is **sharp, severe, and persistent**.

c- Referred Pain:

- It is felt in a region of the body different from the point of its origin because of sharing of common pathways by afferent neurons arising from different sites.

Causes of Abdominal Pain:

1- Inflammation/infection:

a- Peritoneum:

- Chemical and nonbacterial peritonitis: perforated peptic ulcer, gallbladder, or ruptured ovarian cyst.
- Bacterial peritonitis: Primary peritonitis as pneumococcal, streptococcal, or tuberculous.
  Perforated hollow viscus as stomach, intestine, or biliary tract.

b- Hollow intestinal organs:

- Appendicitis
- Gastroenteritis
- Diverticulitis
- Cholecystitis
- Regional enteritis
- Colitis; ulcerative, bacterial, amebic
- Peptic ulceration
- Meckel's diverticulitis

c- Solid viscera:

- Pancreatitis
- Hepatitis and hepatic abscess
- Splenic abscess

d- Mesentery:

- Lymphadenitis.

e- Pelvic organs:

- Pelvic inflammatory disease
- Tubo-ovarian abscess
- Endometritis

2- Mechanical (obstruction, acute distension):

a- Hollow intestinal organs:

- Intestinal obstruction: adhesions, hernia, tumor, volvulus, or intussusception.
- Biliary obstruction: calculi, tumor, choledochal cyst, or hematobilia.

b- Solid viscera:

- Acute splenomegaly
- Acute hepatomegaly: cardiac failure, Budd-Chiari syndrome.

c- Mesentery:

- Omental torsion.

d- Pelvic organs:

- Torsion or degradation of fibroid.
- Ovarian cyst.
- Ectopic pregnancy.

3- Vascular:

a- Intraperitoneal bleeding:

- Ruptured livers.
- Ruptured spleen
- Ruptured mesentery
- Ruptured ectopic pregnancy
- Ruptured aortic, splenic, or hepatic aneurysm.

b- Ischemia:

- Mesenteric thrombosis
- Splenic infarction
- Omental ischemia
- Hepatic infarction: toxemia, purpura.

4- Miscellaneous:

- Endometriosis.

In addition to many extraperitoneal causes of abdominal pain such as pulmonary, cardiac, neurological, metabolic, toxic, infectious, vascular, and hematological causes.

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LIVER & BILIARY TRACT DISEASES

22

• Hepatic physiology and anatomy. • Liver function tests. • Effects of anesthesia on hepatic function. • Liver dysfunction and jaundice (hyperbilirubinemia) in postoperative period or intensive care.	• Hepatitis Acute hepatitis and acute hepatic failure. Chronic hepatitis. • Cirrhosis. • Diseases of the biliary tract. • Hepatic surgery. • Liver transplantation.

Hepatic Physiology and Anatomy

Divisions of the Liver

a. Anatomic Division of the Liver:

Liver is divided by the falciform ligament into larger right and smaller left anatomic lobes. The right lobe has 2 additional smaller lobes at its posteroinferior surface; the caudate and quadrate lobes.

b. Functional (Surgical) Division of the Liver:

Liver is also divided by the point of bifurcation of the hepatic artery and portal vein (porta hepatis) into **total 8 segments**. Therefore, the falciform ligament divides the left surgical lobe into medial and lateral segments.

Hepatic Lobules

• Hepatic lobules are the anatomic unit of the liver. They are about 50 000 – 100 000 in number (figure 22-1). Each lobule is formed of:
  ▫ Plates of **hepatocytes** (liver cells) (endothelial cells) arranged cylindrically around a centri-lobular vein.
  ▫ **Kupffer cells** (macrophages).

• **The acinus** is the functional unit of the liver, formed of a portal tract in the middle and centri-lobular vein at the periphery.
• **The portal tract** is formed of:
  ▫ **A hepatic arteriole**.
  ▫ **A portal venule**.
  The blood of hepatic arterioles and portal venules is mixed in the sinusoidal channels, which lie between the cellular plates and serve as capillaries.
  ▫ **Bile canaliculi**; they originate between hepatocytes and join to form bile duct.
  ▫ **Lymphatics**; they are connected to **the space of Dissé**, which lies between the sinusoids and liver cells.
  ▫ **Nerves** (sympathetic innervations "T_6-T_{11}" and parasympathetic innervations "right and left vagus").

There are about 4-5 portal tracts surrounding each lobule.

• **Hepatic cells** closest to the portal tract (Zone I) are well oxygenated, while those closest to centri-lobular vein (zone III) receive the least O_2 and are most susceptible to injury.

Hepatic Blood Flow

• The liver receives **a dual blood supply** that represents about **25% of cardiac output**. This dual blood supply is formed of:
  ▫ **The portal vein** that supplies **70%** of hepatic blood flow (about 50% of the liver's oxygen supply).
  ▫ **The hepatic artery** that supplies **30%** of hepatic blood flow (about 50% of the liver's oxygen supply also).
• Decreases in systemic blood pressure and cardiac output result in decreased portal vein flow, which can be partially compensated by increased hepatic artery flow. In presence of volatile anesthetics or cirrhosis of the liver, this compensation **(i.e., autoregulation)** is not maintained and may expose the liver to an increased risk of ischemia.

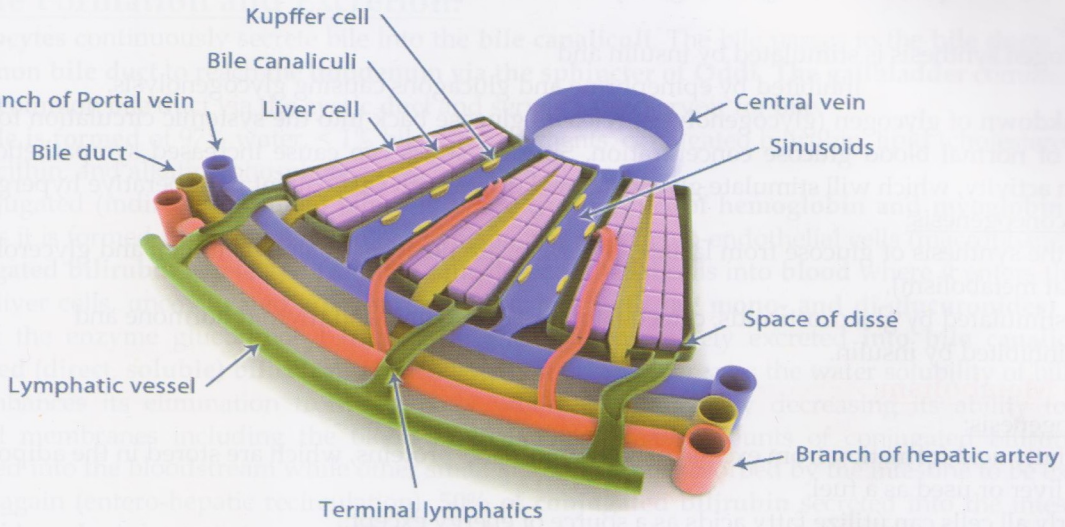


Figure 22-1: Hepatic lobule

- Factors determining hepatic blood flow: include

1- **Hepatic perfusion pressure** = mean arterial or portal vein pressure – hepatic vein pressure.
Therefore, β-blockers such as propranolol decrease portal vein,
positive pressure ventilation of the lungs, congestive heart failure, or fluid overload increase central venous pressure (hepatic vein pressure); therefore, hepatic perfusion pressure and hepatic blood flow are decreased.

2- **Splanchnic vascular resistance**
Splanchnic nerve stimulation by pain, arterial hypoxemia, and surgical stress can increase splanchnic vascular resistance and decrease hepatic blood flow (sympathetic mediated).

Hepatic Functions

The liver performs many functions; vascular functions, metabolic functions, and bile formation and excretion.

I) Vascular Functions of the Liver:

1. Reservoir Function:

The portal vein pressure is normally about **7-10 mm Hg**, but the low resistance of the hepatic sinusoids allows a relatively large blood flow via the portal vein; so, small changes in hepatic venous tone (and pressure) cause large changes in hepatic blood volume allowing **the liver to act as a blood reservoir**. This is explained in the following conditions:

- In hemorrhage, hepatic venous pressure is decreased resulting in the shift of blood (about 300 mL) from the hepatic veins and sinusoids into the venous circulation.
- In congestive heart failure, the central venous pressure is increased resulting in an increase in the hepatic venous pressure; so, the blood accumulates within the liver (about 1000 mL) causing hepatic congestion.

2. Blood Cleansing Function:

Kupffer cells (a part of the reticulo-endothelial system) can perform the following functions:

- They phagocyte (and remove) colonic bacteria, endotoxins, viruses, and cellular debris from the portal circulation.
- They process antigens.
- They release various proteins, enzymes, and cytokines.

II) Metabolic Functions of the Liver:

1. Carbohydrate Metabolism:

1- Glycogen Storage:

- The liver (and to a lesser extent the muscles) can store the absorbed glucose as glycogen. When glycogen storage capacity is exceeded, excess glucose is converted to fat. Glycogen stores are about 70 g while

glucose consumption is average 150 g/day; therefore, glycogen stores are depleted after 24 hours of fasting.

- Glycogen synthesis is stimulated by insulin and inhibited by epinephrine and glucagons causing glycogenolysis.
- Breakdown of glycogen (glycogenolysis) releases glucose back into the systemic circulation for maintenance of normal blood glucose concentration. Surgical stress can cause increased sympathetic nervous system activity, which will stimulate glycogen breakdown with subsequent perioperative hyperglycemia.

2- Gluconeogenesis:

- It is the synthesis of glucose from lactate, pyruvate, amino acids (mainly alanine), and glycerol (derived from fat metabolism).
- It is stimulated by glucocorticoids, catecholamines, glucagons, and thyroid hormone and inhibited by insulin.

2. Fat Metabolism:

1- Lipogenesis:

- It is fatty acid formation from excess carbohydrates and proteins, which are stored in the adipose tissues or the liver or used as a fuel.
- Nearly all cells can utilize fatty acids as a source of energy except:
  - **Red blood cells and renal medulla**, which can only utilize glucose.
  - **Neurons** that can only utilize glucose, but after a few days of starvation, they can utilize fatty acids.
- Lipogenesis is stimulated by insulin.

2- Lipolysis (Fatty Acid Oxidation):

- Lipolysis is the process of oxidation of fatty acids to form acetyl CoA, which has the following roles:
  - It enters citric acid cycle to form adenosine tri-phosphate (ATP).
  - It forms cholesterol and phospholipids, which are used for synthesis of cellular membranes.
  - Excess acetyl CoA forms aceto-acetate (ketone bodies).
- Lipolysis is stimulated by glucagons and inhibited by insulin.

3. Protein Metabolism:

1- Deamination of amino acids i.e. conversion of excess amino acids into carbohydrates and fats (mostly by transaminases) producing ammonia as an end-product. Deamination, especially of glutamine, may also occur to a minor extent in the kidney.

2- Formation of urea, which is excreted by the kidney, by combining 2 molecules of ammonia with CO_2 **to eliminate the ammonia produced from deaminaion** as it is very toxic to the tissues.

3- Inter-conversion between non-essential amino acids to compensate for any dietary deficiency in these amino acids (essential amino acids cannot be synthesized and must be applied exogenously).

4- Formation of plasma proteins (except immunoglobulins) such as:

- Albumin.
- α_1- acid glycoprotein.
- Coagulation factors except factor VIII and Von Willebrand factors. Vitamin K is needed for factor II, VII, IX, and X.
- Plasma cholinesterases, which hydrolyze esters such as some local anesthetics and suxamethonium.
- Protease inhibitors (anti-thrombin III, α_2 antiplasmin, and α_1 antitrypsin).
- Transport proteins (transferrin, haptoglobin, and ceruloplasmin).
- Complements.
- C-reactive protein.
- Serum amyloid A.

4. Drug Metabolism:

Drugs are metabolized to inactive substances or form more water-soluble substances that can be readily excreted in bile or urine. This metabolism is controlled by microsomal enzymes that are present in the smooth endoplasmic reticulum of hepatocytes.

5. Other Metabolic Functions: (hormones, vitamins, and minerals metabolism)

- Degradation of insulin, steroid hormones (estrogen, aldosterone, and cortisol), glucagons, and antidiuretic hormone.
- Formation of more active T_3 from T_4, also their degradation occurs in the liver.
- Site of storage of vitamins A, B_{12}, E, and D.

III) Bile Formation and Excretion:

• **Hepatocytes** continuously secrete bile into the **bile canaliculi**. The bile passes to the **bile ducts** then to the **common bile duct** to reach the **duodenum via the sphincter of Oddi**. **The gallbladder** communicates with the common bile duct via **the cystic duct** and serves as a reservoir for bile.

• **The bile is formed** of 97% water, < 1% bile salts, pigments, conjugated bilirubin, lipid (cholesterol, fatty acids), lecithin, and alkaline phosphate.

• Unconjugated (indirect, insoluble) bilirubin is the end-product of **hemoglobin and myoglobin metabolism** as it is formed from degradation of the heme ring in reticulo-endothelial cells (macrophages). **The unconjugated bilirubin** is released from the reticulo-endothelial cells into **blood** where it enters the liver cells. In liver cells, unconjugated bilirubin is **conjugated (with the mono- and di-glucuronides)** by the action of the enzyme glucoronosyl transferase and is then actively excreted **into bile canaliculi as conjugated (direct, soluble) bilirubin**. This conjugation greatly increases the water solubility of bilirubin, which enhances its elimination from the body while simultaneously decreasing its ability to cross biological membranes including the blood brain barrier. Small amounts of conjugated bilirubin are reabsorbed into the bloodstream while other small amounts are reabsorbed by the intestine to be excreted into bile again (entero-hepatic recirculation). **50% of conjugated bilirubin** secreted into the intestine is converted by colonic bacteria into **urobilinogen**, which reaches the stools and urine (in minor amounts).

Liver Function Tests

Many tests such as serum transaminases reflect hepatocellular integrity more than the hepatic function. Only **serum albumin and prothrombin time (PT)** reflect the hepatic function.

1. Serum Bilirubin:

• Normally, the total bilirubin is **< 1.5 mg/dL** (< 25 µmol/L) (**the direct is < 0.25 mg/dL** and indirect equals the difference between the total and direct bilirubin).

• It reflects the balance between biliary production and excretion.

• **Jaundice** is a clinical diagnosis of yellow pigmentation of sclera and skin resulting from raised plasma bilirubin and is **obvious clinically** when total serum bilirubin **exceeds 3 mg/dL** (40 µmol/L).

• Causes of hyperbilirubinemia are discussed later.

2. Serum Amino-transferase (Transaminases):

• Serum aspartate amino-transferase (AST), previously called serum glutamic-oxaloacetic transaminase (SGOT) is secreted from the **liver, heart, skeletal muscles, and kidneys** while serum alanine amino-transferase (ALT), previously called serum glutamic-pyruvic transaminase (SGPT) is **specific for the liver.**

• Normal serum levels for each enzyme are **<35 - 45 units/L.**

• They are released in response to hepatocellular injury. Absolute levels generally correlate poorly with the degree of hepatic injury.

• Postoperative increased levels may be due to:
  - Skeletal muscle damage by preoperative i.m. injection or by surgery.
  - Hepatocellular injury (they are increased up to 3 times the normal).

3. Serum Alkaline Phosphatase:

• Normal serum level = **45 – 125 units/L.**

• It is present in **the liver, bone, small intestine, kidneys, placenta, and bile duct cells**; so, a slight degree of **biliary obstruction increases its level up to 3 times** the normal. It can differentiate between hepatic dysfunction due to biliary obstruction and due to hepatocellular damage.

• Simultaneous measurement of serum **γ-glutamyl trans-peptidase** (its normal level is 10-40 units/L) is important to exclude extra-hepatic sources of phosphatase elevations such as pregnancy and bone secondaries. Although γ-glutamyl trans-peptidase is released from organs other than the liver (kidneys, heart, lungs, pancreas, intestine, and prostate), the combination of it with increased alkaline phosphatase strongly suggests hepato-biliary disease.

• **5'- Nucleo-tidase** is also measured (but it is increased in late pregnancy too).

4. Serum Albumin:

• Normal serum level = **3.5 – 5.5 g/dL.**

• It is synthesized only in the liver. Its half life is 2-3 weeks; therefore, it may initially be normal with acute liver disease.

• If serum albumin decreases, the free drug fraction increases resulting in an increase in the drug action.

• Values < 2.5 g/dL indicate: ▫ chronic liver disease,

- malnutrition,
- increased loss in the urine e.g., nephrotic syndrome, and
- increased loss in gastrointestinal tract e.g., protein-losing enteropathy.

5. Blood Ammonia:

- Normal serum level = 80 – 110 mg/dL = 47-65 mmol/L.
- If it is markedly increased, it indicates hepatocellular dysfunction due to disruption of hepatic urea synthesis.

6. Prothrombin Time (PT):

- Normal time = 11 – 14 seconds.
- It measures the activity of fibrinogen, prothrombin factors V, VII, and X (i.e., the intrinsic pathway of the blood coagulation cascade).
- It can be corrected by vitamin K.

Effects of Anesthesia on Hepatic Function

A) Effect of Anesthesia on Hepatic Blood Flow (HBF)

1. Regional Anesthesia (Spinal or Epidural):

It **decreases HBF** by about 20-30% due to the reduction of arterial blood pressure.

2. General Anesthesia:

- It **decreases HBF** by also 20-30% due to the reduction of arterial blood pressure and cardiac output resulting in reflex sympathetic stimulation, which in turn causes vasoconstriction of arterial and venous splanchnic vessels.
- All volatile agents **decrease portal vein blood flow** (the greatest reduction is with halothane and the least is with isoflurane). **Autoregulation** of hepatic blood flow (i.e., increased hepatic artery blood flow in response to decreases in portal vein blood flow) is best **maintained with isoflurane, desflurane, and sevoflurane.**

3. Ventilation:

- **Controlled positive pressure ventilation** creates high mean airway pressures that **decrease the HBF** by producing a fall in the venous return, which in turn results in:
  - An increase in the hepatic venous pressure.
  - A decrease in cardiac output that results in reduction of arterial blood pressure and stimulation of the sympathetic system.

Positive end-expiratory pressure (PEEP) further increases these effects.
Therefore, spontaneous ventilation is more advantageous in maintaining the hepatic blood flow.

- **Hypoxemia reduces HBF** due to sympathetic stimulation.
- **CO_2 and pH** produce **variable effects on HBF** due to the following reasons:
  - Direct effects: Hypercarbia and acidosis increase HBF while hypocarbia and alkalosis decrease HBF.
  - Indirect (secondary) effects: Hypercarbia and acidosis stimulate the sympathetic system resulting in decreased HBF.

4. Surgical Procedures near the Liver:

decrease HBF up to 60% due to unclear mechanisms, but it may be due to sympathetic stimulation, local reflexes, and direct vascular compression.

5. Drugs:

- β-blockers, α_1 agonist, H_2 blockers, and vasopressin decrease HBF.
- Dopamine (at the dopaminergic dose) and β agonists increase HBF.

B) Effect of Anesthesia on Metabolic Functions

a. Endocrine Stress Response:

Stress response occurs due to fasting, or surgical trauma. It increases catecholamines, antidiuretic hormone (ADH), glucagons, and cortisol leading to:

- Mobilization of carbohydrates resulting in hyperglycemia.
- Mobilization of proteins resulting in a negative nitrogen balance.

Stress response is partially blunted by regional anesthesia, deep general anesthesia, and pharmacological blockade of the sympathetic system.

b. Drug Metabolism:

Halothane causes:

- Direct inhibition of metabolism of several drugs (such as phenytoin, warfarin, and ketamine).

• Reduction of HBF that alters pharmacokinetics of other drugs (such as fentanyl, verapamil, and propranolol).
• Halothane hepatitis can occur after inhalation of halothane (type I or II). It is discussed in the chapter of "Pharmacology of Anesthesia & Intensive Care".

c. Biliary Function:

• All opioids cause **spasm of sphincter of Oddi** resulting in an increase in the biliary pressure. This causes biliary colic. Opioids are arranged according to their action on sphincter of Oddi as follows: fentanyl and alfentanil (but shorter) > morphine > meperidine > butorphanol > nalbuphine.
• Halothane and to a lesser extent enflurane further increase the biliary pressure after opioids.
• Naloxone and glucagons can relieve the opioid-induced spasm.

Liver Dysfunction and Jaundice (Hyperbilirubinemia) in Postoperative Period or Intensive Care

	Pre-hepatic Causes	Intra-hepatic Causes (Hepatocellular Dysfunction)	Post-hepatic Causes (Obstructive Jaundice)
	Unconjugated (Indirect) Hyperbilirubinemia)	Conjugated (Direct) Hyperbilirubinemia	
Investigations			
• AST (SGOT)	N	↑ to ↑↑↑	N to ↑
• ALT (SGPT)	N	↑ to ↑↑↑	N to ↑
• Alkaline Phosphatase	N	N to ↑	↑ to ↑↑↑
• γ-glutamyl trans-peptidase	N	N to ↑↑↑	↑ to ↑↑↑
• 5′-Nucleo-tidase	N	N to ↑	↑ to ↑↑↑
• Serum Albumin	N	N to ↓↓↓	N to ↓↓↓
• PT	N	↑ to ↑↑↑	↑ to ↑↑↑
• Serum Bilirubin	↑ of **unconjugated** bilirubin	N to ↑↑↑ of **conjugated** bilirubin	N to ↑↑↑ of **conjugated** bilirubin
• Urine analysis	No bilirubin appears	↑ to ↑↑↑ of urinary urobilinogen	↑ to ↑↑↑ of urinary urobilinogen
Causes	**a- An increase in bilirubin production:** • **Large hematoma** reabsorption (the most common cause) • **Hemolysis** (indicated by a decrease in hematocrit or an increase in reticulocytic count) e.g., drugs, malaria, hemolytic uremic syndrome, sickle cell anemia, glucose-6-phosphate dehydrogenase deficiency syndrome. • **Blood transfusion** due to **acute hemolytic or delayed hemolytic reactions or just increased unconjugated bilirubin load** as blood transfusion of one unit of blood contains about 250 mg of bilirubin, which increases as the age of the transfused blood increases. **b- Decreased conjugation of bilirubin:** such as **Gilbert's syndrome** and Grigler-Najjar 2syndrome where both syndromes have a specific defect in the glucoronosyl transferase enzyme.	**a- Mild postoperative liver dysfunction** may occur in a healthy person due to **the reduction of HBF** by anesthesia, surgical procedures near the liver, and sympathetic stimulation. **b- Acute or chronic hepato-cellular dysfunction:** such as • Viruses as A, B, C, Epstein-Barr. • Toxoplasmosis. • Sepsis. • Drug-induced as paracetamol (common), halothane, or alcohol. • Arterial hypoxemia (ischemic injury). • Cirrhosis. • Congestive heart failure. **c- Intra-hepatic cholestasis (decreased canaliculi transport of bilirubin):** • Benign postoperative intra-hepatic cholestasis (see later). • Infection. • Drug-induced such as cephalosporins, carbamazepine, or erythromycin.	**Extra-hepatic cholestasis (obstruction of the bile ducts):** such as • Postoperative cholecystitis. • Pancreatitis. • Retained common bile duct stone. • Neoplasm. • Sepsis. Ultrasound and CT scan will diagnose extra-hepatic biliary obstruction and may show dilated common bile duct.

N = normal, ↑ = mild increase, ↑↑ = moderate increase, ↑↑↑ = marked increase, and ↓↓↓ = marked decrease

Benign Postoperative Intra-hepatic Cholestasis:

- It occurs after prolonged surgery, especially if it is complicated by hypotension, hypoxemia, and the need for blood transfusion.
- There is an increase in bilirubin production (breakdown of transfused red cells or resorption of a hematoma) and/or decreased hepatic clearance of conjugated bilirubin, but with normal conjugation resulting in conjugated hyperbilirubinemia (and jaundice) which usually resolves within several days postoperatively.

Diseases of Liver and Biliary Tract

They are categorized as:

- Parenchymal liver disease: ▫ hepatitis (acute and chronic)
  ▫ cirrhosis.
- Cholestasis: ▫ intra-hepatic.
  ▫ extra-hepatic.

Hepatitis

A) Acute Hepatitis and Acute Hepatic Failure

Definition

Acute hepatitis: is acute inflammation of the liver that lasts less than 6 months

Acute liver Failure: is massive damage to liver cells leading to severe rapid deterioration of the liver function.

Acute fulminant liver failure: is acute hepatic failure with superimposed hepatic encephalopathy that develops within 2 to 8 weeks of the onset of illness.

Causes

1- Viral Hepatitis: is the most common cause. Hepatitis viruses A, B, C, D, and E are the most common viruses that produce hepatitis. Other viruses include epstein-Barr, herpes simplex, cytomegalovirus, and coxsackie virus.

2- Exposure to Hepato-toxins and Drugs (Drug-induced Hepatitis):

- **Toxic** (at overdoses): such as acetaminophen, alcohol, vinyl chloride, trichloroethylene, poisonous mushrooms (Amanita phalloides), salicylates, carbon tetrachloride, yellow phosphorus, or tetracycline.
- **Idiosyncratic** (at any dose): such as volatile anesthetic (halothane), phenytoin, sulfonamides, rifampicin, or indomethacin.
- **Toxic and idiosyncratic**: such as methyldopa, isoniazid, sodium valproate, or amiodarone.
- **Primary cholestatic**: such as chlorpromazine, chlorpropamide, oral contraceptives, cyclosporine, anabolic steroid, erythromycin, methimazole.

3- Miscellaneous Causes:

- Acute fatty liver of pregnancy.
- Hepatic ischemia.
- Budd-Chiari syndrome.
- Reye's syndrome.
- Autoimmune hepatitis
- Wilson's disease.
- Decompensation of chronic liver disease due to infection or variceal bleeding.

Clinical Picture

It ranges from **asymptomatic** mild increase in serum transaminases up to **acute hepatic failure.**

- Prodroma of 1-2 weeks duration is usually present in the form of **flu-like symptoms** such as fatigue, malaise, anorexia, low-grade fever, headache, nausea, and vomiting, which usually occur in a previously healthy individual.
- Jaundice usually occurs after the prodroma, lasts 2-12 weeks and is associated with **dark urine** (94%), **light-colored stools, and pruritis.**
- Hypotension and decreased systemic vascular resistance (**hyperdynamic circulation**) may occur and may progress to **oliguric renal failure (hepatorenal syndrome)** in some patients.
- Acute encephalopathy may occur in acute fulminant hepatic failure.
  - **The interval between** the development of **jaundice and the onset of encephalopathy** has been used to classify hepatic failure as hyperacute (0-7 days), acute (8-28 days), and subacute (28 days -12 weeks).

▫ **The severity of encephalopathy** is measured in 4 stages:

Stage/Grade	Mental Status	Tremors	Brain Edema and increased intracranial tension	Electroencephalography
I	Euphoria, occasionally depression; fluctuating mild confusion; slowness of mentation and affect; slurred speech; disorder in sleep rhythm.	Slight	Absent	Normal
II	Drowsiness; inappropriate behavior	Present	Absent	Generalized slowing
III	Sleeps most of the time (i.e. stuporous), but is arousable, very confused, incoherent speech, and agitated.	Present	Usually present	Abnormal
IV	Unarousable, unresponsive to painful stimuli (coma).	Absent	Present	Abnormal

▫ This classification of encephalopathy can be applied for both acute and chronic hepatitis, but **only in acute hepatitis, there is cerebral edema and increased intracranial tension.** The risk of cerebral edema and increased intracranial tension is higher at grades 3 and 4 (50-80%) manifested by systemic hypertension, progressive bradycardia, and increasing muscle rigidity at intracranial tension > 30 mm Hg with risk of brain herniation. CT scan and intracranial tension monitoring are helpful.

▫ Causes of encephalopathy and brain edema:

1- Failure of hepatic clearance, which causes accumulation of toxins such as ammonia and manganese.

2- Alteration in endogenous neurotransmitters e.g., γ-amino-butyric acid (GABA), glutamate, and nitric oxide.

3- Absence of enzymes of the urea cycle in the brain, which results in glutamine accumulation (glutamine is a substrate for the urea cycle). It is an osmotic compound leading to cerebral edema (only in acute liver failure). In chronic liver failure, glutamine accumulates, but compensatory changes prevent edema formation.

4- Sodium accumulation in the brain cells due to inhibition of Na^+-K^+-ATPase enzyme.

- **Features of Viral Hepatitis:**

	Virus A	Virus B	Virus C	Virus D
Mode of transmission	• Feco-oral route (virus E is transmitted also by feco-oral route)	• Percutaneous • Sexual • Contact with body fluids • Maternal-infant transmission.	• Percutaneous • Contact with body fluids • Maternal-infant transmission.	• Percutaneous • Sexual (usually with virus B)
Incubation Period	20-37 days	60-110 days	35-70 days	60-110 days
Immunity	• **Ig M** appears early and persists for 120 days. • **Ig G** appears during convalescence and persists indefinitely thereby conferring immunity.	• **Hepatitis B surface antigen (HBsAg)** appears early 7-14 days after infection and persists in infectious carriers for several months indicating active virus replication • **Antibody to HBsAg (anti- HBsAg)** appears in blood 60-240 days after infection by which time the HBsAg is undetectable and persists indefinitely thereby conferring immunity. • **Antibody to the core antigen of HB virus (anti-HBc)** appears promptly (early) after infection and persists for 6-12 months.	• **Antibody to hepatitis C virus (anti-HCV)** appears in 6 weeks to 9 months. • **Hepatitis C viral RNA** is used to detect and confirm infectious carriers. It is detected in peripheral blood by polymerase chain reaction (PCR).	• **Antibody to hepatitis D virus (anti-HDV)** appears late and may be short-lived.

Course of the Disease	• Complete recovery occurs and does not progress to chronic liver disease. • No infectious carriers are present	• It progresses to chronic liver disease in 1-5% of adults and 80-90% of children. • Infectious carriers occur in 0.3-30% of cases.	• It progresses to chronic liver disease in 60-70% of cases. • Infectious carriers occur in 0.5-1% of cases.	• Co-infection with type B is common.
Prevention after exposure	• Pooled γ-globulin is given within 14 days. • Hepatitis A vaccine.	• Hepatitis B immunoglobulin (0.06 mL/kg) is given intra-muscularly within 24 hours. • Hepatitis B vaccine (3 doses; the first 2 doses given by deep intramuscular injections are given 4 weeks apart and the third dose is given 5 months after the second dose).	Actually no effective prophylaxis is available • Interferon and hepatitis immunoglobulin are tried but not effective.	• Unknown.

Treatment of Acute Hepatitis and Acute Hepatic Failure

1- Treatment of the cause (if possible) is very important e.g., an antidote for acetaminophen toxicity as N-acetylcysteine, which is given as follows:

Loading dose: 150 mg/kg i.v. infused over 1 hour diluted in 250 mL 5% glucose.
First maintenance dose: 50 mg/kg i.v. infused over 4 hours diluted in 500 mL 5% glucose.
Second maintenance dose: 100 mg/kg i.v. infused over 16 hours diluted in 1000 mL 5% glucose.
Continuing treatment: consider 150 mg/kg over 24 hours until liver failure improves or transplantation takes place.
Total treatment hours are 21 hours.

2- Supportive treatment: such as

- **I.v. glucose** for hypoglycemia.
- **I.v. fluids** for volume replacement and avoiding renal failure.
- **I.v. vasopressors** for the hyperdynamic circulations.
- **Vitamin K and fresh frozen plasma** for the associated coagulopathy.
- **Mechanical ventilation and intubation** for airway protection and hepato-pulmonary syndrome (see later).
- **Brain protection and measures to decrease intracranial tension** such as mannitol, head elevation, hypothermia, and thiopentone (controversial due to its delayed metabolism owing to liver insufficiency). Corticosteroids are not indicated.
- **Dialysis** for renal failure.

No specific treatment is available for acute hepatitis or acute liver failure.

3- Liver transplantation: when survival seems unlikely, the only curative treatment is **liver transplantation**.

Predictors of Poor Outcome in Patients with Acute Hepatic Failure (King's College Criteria): These criteria indicate those unlikely to survive without transplantation. They are categorized according to the cause of acute hepatitis as follows:

- **Acetaminophen Toxic Patients:**
  - Blood pH < 7.3 (irrespective of grade of encephalopathy) or
  - A combination of encephalopathy stage III or IV, prothrombin time > 100 seconds (international normalized ratio "INR" > 6.5), and serum creatinine > 3.4 mg/dL (> 200 μmol/L).
- **Non-acetaminophen Toxic Patients:**
  - Prothrombin time > 100 seconds (INR > 6.5) (irrespective of stage of encephalopathy) or
  - Any three of the following five variables (irrespective of stage of encephalopathy):
    1- Age < 10 years or > 40 years.
    2- Etiology: hepatitis C, halothane hepatitis, Wilson's disease, idiosyncratic drug reaction.
    3- Duration of jaundice before onset of encephalopathy of > 7 days.
    4- Prothrombin time > 50 seconds (INR > 3.5).
    5- Serum bilirubin level of > 17.5 mg/dL (> 300 μmol/L).

Anesthetic Management

Preoperative Management:

• **Postpone all elective surgeries** until resolving of acute hepatitis (indicated by normal liver function tests) as it increases the mortality and morbidity. Only emergency surgeries should be done during acute hepatitis.

• Assess **the cause and degree** of hepatic impairment e.g., recent drug, alcohol…etc.

• Assess **mental status** as mental changes indicate severe hepatic impairment.

In alcoholic patients, acute toxicity causes inappropriate behavior while acute withdrawal causes tremulousness and irritability **(tremens delirium).**

Preoperative Investigations:

1- **Hepatitis Markers** (as above).

2- **Liver function tests:**

• **AST and ALT** concentrations increase 7 to 14 days before the appearance of jaundice and begin to decrease shortly after jaundice develops. Although AST and ALT are sensitive indicators of liver cell injury, their increase does not necessarily parallel the severity of hepatitis, but concentrations less than 500 IU/L usually reflect mild hepatitis. **ALT (specific) is generally > AST** except in alcoholic hepatitis in which the reverse occurs where AST: ALT ratio is at least 2: 1 because there is increased synthesis and secretion of AST into plasma and selective loss of ALT due to the pyridoxine deficiency that is common in alcoholism.

• **Serum bilirubin and alkaline phosphatase** are usually moderately increased except with the cholestatic type of hepatitis where they become markedly increased.

• **Prothrombin time** is increased; it is the best indicator for hepatic synthetic function. If it is persistent > 3 seconds above normal after vitamin K injection, this indicates severe hepatic dysfunction.

3- **Serum electrolytes and arterial blood gases** show hypokalemia and metabolic acidosis due to vomiting.

4- **Serum blood sugar** shows hypoglycemia; so, glucose infusion is needed.

5- **Serum albumin** shows hypoalbuminemia, only if **there is chronic liver** disease or **malnutrition**.

All these anesthetic problems should be corrected before induction of anesthesia.

Premedications:

• **Avoid** premedications as **they may precipitate hepatic encephalopathy** in patients with severe liver disease.

• **Benzodiazepines and thiamine should be given for alcoholic patients with acute withdrawal.**

• **Preoperative lactulose therapy** may be given to decrease ammonia load and prevent development of hepatic encephalopathy.

Intraoperative Management:

• **Extra-caution** is indicated in avoiding contact with blood and body fluids from these patients by gloves, masks, protective wear to eyes and by avoiding recapping needles. Also vaccination is recommended (against B).

• **The doses of anesthetics** should be adjusted according to the patient's status as follows:

▫ Patients with **viral hepatitis** have increased neurological sensitivity to anesthetics; therefore, doses of anesthetics should be **decreased**.

▫ Patients with **chronic alcoholic toxicity** show cross-tolerance (resistance) to anesthetics due to hepatic enzyme induction; therefore, doses of anesthetics should be **increased**.

▫ Patients with **acute alcoholic toxicity** show neurological depression; therefore, doses of anesthetics should be **decreased**.

Choice of Anesthesia

a. Regional Anesthesia: can be used provided that, there is no coagulopathy or hypotension.

b- General Anesthesia:

Induction: is performed by i.v. agents with **standard doses** because the action of i.v. anesthetic agents is terminated by **redistribution** rather than metabolism or excretion; so, **there is no fear of prolonged action**, but **large and repeated doses** should be **avoided** (especially opioids and thiopentone) due to hangover and cumulation, which prolong the action.

Succinylcholine is used **safely** without a prolonged response because half-life of plasma cholinesterase is 14 days; so, it is unlikely to be affected in acute liver disease.

Maintenance:

- All inhalational anesthetic agents are metabolized in the liver producing trifluoro- acetic acid (TFA), which produces harmful effects on the liver except sevoflurane, which is metabolized in the liver producing hexa-fluoro-isopropanol (HFIP). HFIP is not toxic on the liver; therefore, **sevoflurane is of choice** in patients with liver impairment.
- **Isoflurane and sevoflurane** have the least effects on HBF.
- Avoid factors which decrease HBF as hypotension, sympathetic stimulation, and high mean airway pressure during controlled ventilation.

Fluid Therapy:

- Glucose should be given to avoid hypoglycemia in patients with liver impairment.
- Urine output should be maintained with fluids and diuretics.

B) Chronic Hepatitis

Definition

It is persistent hepatic **inflammation ≥ 6 months** as evident by increased amino-transferases with/without liver biopsy.

Types (according to the liver biopsy)

1. Chronic Persistent Hepatitis:

Biopsy: shows **chronic inflammation of portal tracts** with preservation of **normal** cellular architecture.
Clinical picture: ▫ Acute hepatitis (B and C), which lasts > 6 months and eventually resolves.
▫ It does not usually progress to cirrhosis.

2. Chronic Lobular Hepatitis:

Biopsy: shows **foci** of chronic inflammation and **necrosis** in hepatic lobules.
Clinical picture: ▫ Acute hepatitis that resolves, but it is followed by recurrent exacerbations.
▫ It does not usually progress to cirrhosis.

3. Chronic Active Hepatitis:

Biopsy: shows chronic inflammation with **destruction** of normal cellular architecture **(i.e., piecemeal necrosis).**
Clinical picture:

- ▫ Chronic hepatitis after hepatitis B and C or with drugs as methyldopa, isoniazid, aspirin and dantrolene.
- ▫ Fatigue, recurrent jaundice, and mild increases in serum amino-transferases.
- ▫ Extra-hepatic autoimmune disorders as diabetes mellitus, thyroiditis, arthritis, serositis, myocarditis, glomerulonephritis, and thrombocytopenia.
- ▫ Cirrhosis in 20-50% of patients.
- ▫ Treated by corticosteroids or azathioprine, if no HBsAg is present.

Anesthetic Management

- Chronic persistent and chronic lobular hepatitis are managed as acute hepatitis.
- Chronic active hepatitis is managed as cirrhosis (see later), in addition to management of extra-hepatic disorders such as diabetes mellitus, thyroiditis….etc.

Cirrhosis

Causes

A- Non-Cholestatic Causes:

- **Laennec's** cirrhosis due to alcohol (the most common cause in western countries).
- **Post-necrotic** cirrhosis due to:
  - ▫ **chronic active hepatitis B and C** (infectious) (the most common cause in developing countries),
  - ▫ **autoimmune hepatitis**, or
  - ▫ **cryptogenic hepatitis** (unknown cause).
- **Cardiac** cirrhosis due to right-sided congestive heart failure.
- **Metabolic** cirrhosis due to:
  - ▫ Hemochromatosis (deposition of iron in hepatocytes; autosomal recessive disorder).
  - ▫ Wilson's disease (deposition of copper in hepatocytes; autosomal recessive disorder).

- α_1 antitrypsin deficiency (usually with pulmonary emphysema).
- Amyloidosis.
- Cystic fibrosis.

B- Cholestatic Causes:

• **Biliary** cirrhosis due to chronic biliary inflammation or obstruction e.g., primary biliary cirrhosis (an autoimmune disease) or primary sclerosing cholangitis.

Pathophysiology

Pathophysiology of liver cirrhosis is summarized in figure 22-2.

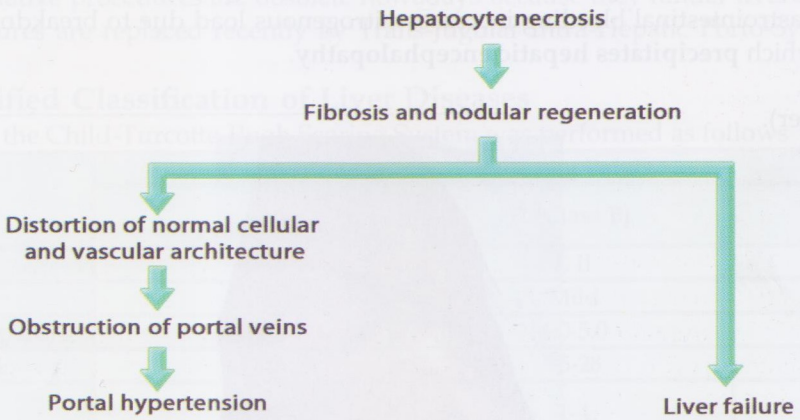


Figure 22-2: Pathophysiology of liver cirrhosis

N.B.: Causes of Portal Hypertension without Liver Failure:

1- Schistosomiasis because it produces fibrosis.
2- Idiopathic portal fibrosis (Banti's syndrome).
3- Congenital hepatic fibrosis.
4- Obstruction of hepatic veins or inferior vena cava (Budd-Chiari syndrome) due to:
- Hypercoagulability resulting in venous thrombosis.
- Tumor thrombi as in renal carcinoma.
- Occlusive disease of sub-lobular hepatic veins.

Clinical Pictures of Cirrhosis

Signs and symptoms often do not correlate with the disease severity. Fatigue, malaise, palmar erythema, gynecomastia, testicular biopsy, and spider angiomata are common. Clinical picture is absent initially, but jaundice and ascites eventually develop in most patients.

Investigations

1- Percutaneous liver biopsy.
2- Computerized tomography imaging (CT scan).
3- Magnetic resonance imaging (MRI).
4- Hepatic ultrasonography with Doppler flow studies, which may reveal signs of splenomegaly, ascites, and irregular liver surface.
5- Upper gastrointestinal endoscopy for varices.
6- Decreased serum albumin, prolonged prothrombin time, increased serum amino-transferases, and alkaline phosphatase enzyme.

Preoperative Management (and Intensive Care Management)

The **cause** of cirrhosis should be assessed and managed as possible.

Clinical Pictures and Complications of Liver Cirrhosis:

1. Gastrointestinal System:

A) Portal Hypertension:

Definition: It is defined as a **pressure gradient > 10 mm Hg** between **the portal vein and the inferior vena cava** (the pressure gradient is 2-6 mm Hg normally).

Causes: High resistance to blood flow through the liver causes an accumulation of blood in the vascular beds that are immediately upstream from the liver. Venous drainage of the esophagus, stomach, spleen, and intestine dilates and increases in capacity, which leads to the development of splenomegaly, esophageal, gastric, and intra-abdominal varices.

Clinical Picture:

- Extensive porto-systemic venous collaterals that permit passage of splanchnic venous blood from the high-pressure portal venous system to the low-pressure azygos and hemi-azygos veins. These collaterals are manifested as **gastro-esophageal varices**, **hemorrhoids**, veins around the umbilicus **(Caput Medusae)** (figure 22-3), and intra-abdominal and retroperitoneal varices.
- Gastro-esophageal varices may cause **acute massive bleeding** which is a major cause of morbidity and mortality. Gastrointestinal bleeding increases nitrogenous load due to breakdown of blood in the intestinal tract, which **precipitates hepatic encephalopathy**.
- **Splenomegaly.**
- **Ascites** (see later).



Figure 22-3: Caput Medusae

Preoperative Treatment:

1- ABCDE resuscitation in shocked patients.

2- Esophago-duodenoscopy or arteriography for diagnostic and therapeutic management as endoscopic sclerotherapy or endoscopic band ligation.

3- Pharmacological therapy such as octreotide, i.v. propranolol, and i.v. nitroglycerin.

4- Balloon tamponade such as Sengstaken-Blakemore tube.

5- Surgical treatment in severe and recurrent cases.

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The details of treatment are discussed in chapter "Gastro-intestinal Disease".

B) Assessment of the Degree of Hepatic Impairment.

This is important to assess the degree of severity and hepatic reserve.

Child-Turcotte-Pugh Scoring System has used to determine the patients at high risk (those with high score). These patients are scheduled first to have a liver transplantation. This score is replaced later on by the MELD and PELD score (see later).

Points	1 Point	2 Points	3 Points
1. Serum bilirubin (mg/dL) **N.B.:** For **cholestatic liver diseases** as primary biliary cirrhosis and primary sclerosing cholangitis, bilirubin values (mg/dL) are substituted by	< 2.0 < 4	2.0 – 3.0 4-10	> 3.0 > 10
2. Serum albumin (g/dL)	> 3.5	2.8 – 3.5	< 2.8
3. Ascites	None	Slight and controlled by diuretics	Moderate to severe and poorly controlled by diuretics
4. Encephalopathy (coma)	None	Minimal (stage 1-2)	Advanced (stage 3-4)
5. Prothrombin time (seconds above the control) Or **INR**	1-4 or < 1.7	4-6 or 1.7-2.3	> 6 or > 2.3

N.B.: This classification was first proposed by "Child" as a means of predicting the operative risk (morbidity and mortality) associated with porto-caval shunt surgery. The original Child classification used nutrition instead of the prolongation of the prothrombin time.

- Child class A patients (= 5-6 points with mortality 10%) are low-risk patients and can undergo shunting procedures such as nonselective shunts (porto-caval and proximal spleno-renal) or selective shunts (distal spleno-renal) which are the best with less encephalopathy.
- Child class B patients (= 7-9 points with mortality 30%) are intermediate-risk patients.
- Child class C patients (= 10-15 points with mortality 75%) are high-risk patients and can undergo ablative surgery such as esophageal transection or gastric devascularization.

The shunt and ablative procedures are obsolete nowadays because they hinder liver transplantation later on. These procedures are replaced recently by Trans-Jugular Intra-Hepatic Porto-Systemic Shunt (TIPS) Procedure.

Moemen Modified Classification of Liver Diseases

A modification of the Child-Turcotte-Pugh Scoring System was performed as follows

Variables	Scoring Points		
	1 (Class A)	2 (Class B)	3 (Class C)
Encephalopathy	0	I, II	III, IV
Ascites	0	Mild	Moderate, severe
Serum bilirubin (mg/dL)	< 4.0	4.0-5.0	> 5.0
Serum albumin (g/L)	> 35	35-28	< 2.8
Prothrombin Time prolonged (seconds)	0	1-4	> 4
Serum Sodium (mmol/L)	> 130	130-120	< 120
Serum creatinine (mg/dL)	< 1.5	1.5-2.5	> 2.5
Leucocytic count ($10^3/mm^3$)	< 10	10-12	> 12
Arterial/alveolar oxygen tension ratio	≥ 0.75	0.74-0.55	< 0.55

The surgical risk is classified according to the scoring points into: mild (9-10 points), moderate (11-14 points) and severe (15-27 points).

Trans-Jugular Intra-Hepatic Porto-Systemic Shunt (TIPS) Procedure:

TIPS procedure involves angiographically placing **an expandable stent** into the liver parenchyma between a hepatic vein and a portal vein to provide a porto-systemic communication and to decompress the portal circulation and treat refractory ascites. It is performed under local or general anesthesia and is often used as **a bridge to liver transplantation.**

Advantages:

It does not require abdominal operation or vascular division; so, **it carries no technical hazards to the future liver transplantation**, unlike older surgical porto-systemic procedures e.g., spleno-renal shunts.

Disadvantages (Complications):

Bleeding, infection, hemobilia, stent migration, worsened encephalopathy due to enhanced systemic delivery of biogenic amines normally cleared by the liver and its long-term patency is poor needing revisions.

2. Circulatory System:

Clinical Picture:

1- **Hyperdynamic circulatory state:** may occur due to the following reasons:

- Presence of **arteriovenous shunts** in systemic and portal circulation.
- Presence of **physiological shunting** where the blood passes from the arterial to the venous side of the circulation without effectively traversing a capillary bed due to peripheral and splanchnic vasodilation because vasodilator substances e.g., NO and glucagon will bypass the normal hepatic metabolism)
- Presence of **anatomic shunts** where there are abnormal blood vessels, such as those seen in the skin as spider angiomas.
- Decreased blood viscosity due to presence of anemia, which leads to a high cardiac output.

Hyperdynamic circulation resolves after liver transplantation by several years.

2- **Alcoholic cardiomyopathy** with congestive heart failure may occur due to chronic alcohol intake.

3- **Arrhythmias** due to electrolyte and acid base disturbances.

3. Hematological System:

Clinical Picture:

1- **Anemia** due to repeated blood loss, red blood cells destruction, bone marrow depression, and nutritional deficiency.

2- **Thrombocytopenia**, **thromboasthenia**, and **rarely leucopenia** due to congestive splenomegaly (hypersplenism) from portal hypertension.

3- **Coagulation factor deficiencies** due to decreased hepatic synthesis and decreased vitamin K absorption, but fibrinogen and factor VIII are not decreased, as they are not synthesized in the liver.

4- **Increased fibrinolysis** due to decreased clearance of tissue plasminogen activators of the fibrinolytic system and decreased levels of antiplasmin.

Preoperative Treatment:

1- **Preoperative transfusion** to increase Hct up to 30% when blood loss is expected during surgery but increased nitrogen load should be avoided as this precipitates encephalopathy.

2- **Preoperative platelet count** should be assessed.

3- **Preoperative coagulation screen and thromboelastography** can assess the overall clotting and platelet function and fibrinolysis.

Any coagulopathy should be corrected preoperatively by **fresh frozen plasma, platelet** transfusion (if platelets are < 100 000/μL) and **cryoprecipitate** (in severe cases).

4- Avoid i.m. injections for premedication.

4. Respiratory System:

1- Hepato-pulmonary Syndrome:

It is a triad of **liver disease, intra-pulmonary vascular dilatation, and arterial hypoxemia** in absence of intrinsic lung diseases.

Mechanism:

- It is due to unknown cause, but there may be an increased production and a decreased hepatic clearance of **endogenous vasodilators** e.g., NO.
- Arterial **hypoxemia occurs** due to:
  - Increased right-to-left intrapulmonary shunting (absolute) because of portal hypertension.
  - Increased ventilation/perfusion mismatching (relative).
  - Impaired movement of diaphragm because of accumulation of ascitic fluid.

N.B.: A contrast (or bubble) echocardiography is useful to define the cause of room air hypoxemia. After venous injection of the contrast (or small bubbles):

- If micro-bubbles are seen immediately in the left atrium, it is a cardiac shunt.
- If micro-bubbles are seen 5-6 beats after injection in the left atrium, it is an intra-pulmonary shunt.
- If micro-bubbles are not seen as they are absorbed in the lung, it is a ventilation/perfusion defect.

Clinical Picture of Hepato-pulmonary Syndrome:

There are dyspnea, fatigue, clubbing, platypnea (i.e., shortness of breath occurring in the upright position), and orthodeoxia (i.e., arterial deoxygenation occurring in the upright position).

It is **not a contra-indication for liver transplantation**; on the contrary, its **resolution may occur after** transplantation.

2- Decreased lung volumes (especially functional residual capacity) due to elevation of the diaphragm by ascites and pleural effusion (hepatic hydrothorax) which results in **atelectasis** and **restrictive lung disease**.

3- Primary respiratory alkalosis due to hyperventilation.

4- Pulmonary hypertension may occur in about 2% of patients with chronic liver disease.

Preoperative Treatment:

1- Paracentesis to decrease the ascites.

2- Chest x-ray and arterial blood gases to detect hypoxemia and atelectasis.

5. Renal System:

Hepato-renal Syndrome:

Definition: It is a functional renal defect (acute renal failure) occurring in patients with preexisting chronic liver failure and without a primary intrinsic renal disease.

Mechanism of Hepato-renal Syndrome: It is not clear, but it may be due to:

- Increased endothelin (and increased sympathetic tone) which causes afferent arteriolar vasoconstriction (other vasoactive mediators are also involved such as angiotensin II, norepinephrine, neuropeptide Y, adenosine, and leukotrienes).
- Increased NO and prostaglandins which cause efferent arteriolar vasodilation, in addition to splanchnic vasodilation.

Both lead to under-filling of the arterial circulation and renal hypoperfusion resulting in decreased glomerular filtration rate.

Precipitating Factors: are gastrointestinal bleeding, bacterial peritonitis, overzealous use of diuretics to control ascites, or major surgery.

Clinical Picture (Diagnosis): It is diagnosed by:

- Absence of a primary intrinsic renal disease.
- Two types of hepato-renal syndromes are recognized:

  Type I: is characterized by **rapid and progressive** impairment of renal function. Dominant features are marked renal failure, oliguria or anuria, and high level of urea and creatinine. Most patients have hyperbilirubinemia, coagulopathy, and encephalopathy. The median survival is only 2 weeks.

  Type II: is characterized by **mild and stable** reduction in renal function. These patients typically present with diuretic-resistant ascites.

Investigations:

- Serum creatinine is > 1.5 mg/dL.
- Creatinine clearance is < 40 mL/min.
- Urine analysis shows bile-pigmented cast, proteinuria, and urinary Na^+ is < 10 mEq/L.
- Urine: Plasma creatinine ratio is extremely high.
- Fractional Na^+ excretion is < 1%.
- Functional urea excretion is < 20%.

Preoperative Treatment: (of hepato-renal syndrome) is only supportive.

1. **Preoperative hydration** with i.v. infusion for at least 12 hours before surgery. I.v. saline and albumin may aggravate ascites; therefore, whole blood or packed red blood cells may be a more appropriate form of volume replacement.
2. Avoid nephrotoxic drugs such as cyclosporine and contrast dyes.
3. **Immediate preoperative mannitol 100 mL** to prevent renal failure. It may be given **postoperatively** if the urine output is < 50 mL/hour.
4. **I.v. clonidine** can decrease renal vascular resistance and improve glomerular filtration rate by as much as 50%.
5. **Vasoconstrictors such as terlipressin or vasopressin analogues** can improve splanchnic vasodilation, decrease endogenous vasoconstrictor levels, and improve renal blood flow, but it may decrease cerebral blood flow in patients with acute hepatic necrosis.
6. **The combined use of midodrine** (an α_1 adrenergic agonist) and **octreotide** (a somatostatin analogue) may improve renal hemodynamics.
7. The only hope is **liver transplantation** if hepato-renal syndrome occurs. In severe renal failure, **combined liver-kidney transplantation** is needed.

6. Fluid and Electrolyte Balance:

1. Ascites: is common due to the following reasons:

- **Portal hypertension** increases the hydrostatic pressure, which favors transudation of fluid across the bowel.
- **Hypo-albuminemia** decreases the oncotic pressure.
- **Seepage of protein-rich lymphatic fluid** from the serosal surface of the liver. It may be secondary to distortion and obstruction of lymphatic channels in the liver.
- **Renal Na^+ (and often H_2O) retention** may occur explained by 2 theories:
  - **Under-filling** theory: It proposes that although the measurable total extracellular fluid (ECF) and plasma volume are increased (due to the increase in splanchnic blood volume) in cirrhotic patients with ascites, effective plasma volume is decreased; so, Na^+ retention occurs **secondary to relative hypovolemia and secondary hyperaldosteronism.**
  - **Over-flow** theory: It proposes that the **primary abnormality in Na^+ retention is in the kidney** (increase in proximal and distal Na^+ reabsorption). This expands plasma volume resulting in transudation and ascites.

Investigations:

- **Diagnostic paracentesis of ascites** (due to portal hypertension) reveals clear, straw-colored fluid.
- **The serum-to-ascites albumin gradient**, calculated by subtracting the ascitic fluid-albumin level from the serum albumin level, has been shown to be effective in differentiating portal hypertensive from non-portal hypertensive ascites. Patients with a gradient of more than 1.1 g/dL can be diagnosed to have portal hypertension with a reliability of 97%. A gradient of less than 1.1 g/dL suggests non-portal hypertensive etiology.
- **Ultrasonography or CT scanning** is helpful in detecting even small volumes of ascitic fluid.
- **Duplex ultrasound** of the portal and hepatic venous system is indicated if portal vein thrombosis or hepatic vein thrombosis is suspected.

2. Hypoglycemia reflects glycogen depletion due to malnutrition. The liver is responsible for clearing lactic acid from systemic circulation and then converting lactate to glucose; so, liver impairment causes hypoglycemia and **lactic acidosis**.

3. Electrolyte disturbances such as:

- **Hyponatremia** due to dilution, increased antidiuretic hormone, impaired renal handling of free-water and decreased Na^+ in diet.
- **Hypokalemia** due to increased renal K^+ losses (because of diuresis or secondary hyperaldosteronism).
- **Hyperkalemia** due to K-sparing diuretics, renal failure, and metabolic acidosis.
- **Hypomagnesemia** due to poor dietary intake, intestinal malabsorption, hyperaldosteronism, and diuretic therapy.

4. Acid-Base Disturbances:

- **Respiratory alkalosis** (the most common) due to hyperventilation.
- **Metabolic alkalosis** due to loop diuretics, hyperaldosteronism, vomiting, or diarrhea.
- **Metabolic acidosis** in critically ill patients especially those with renal failure.

Preoperative Treatment:

1- Judicious preoperative fluid transfusion because acute i.v. fluid deficits should be corrected with colloid infusions.

2- Avoid aggressive preoperative diuresis. Loop diuretics (furosemide) are only given when the patient is bedridden.

- Na^+ restriction (< 2 g NaCl/day) and spironolactone are ineffective.
- Daily body weight measurements are needed to avoid i.v. volume depletion during diuresis.
  - For patients with ascites and peripheral edema, no more than 1 kg/day should be lost on diuresis.
  - For patients with ascites alone, no more than 0.5 kg/day should be lost on diuresis.

3- Treatment of electrolyte disturbances such as:

- Treatment of hyponatremia < 130 mEq/L is by water restriction.
- Treatment of hypokalemia < 3.5 mEq/L is by preoperative K^+ replacement.
- Treatment of hypoglycemia < 80 mg/dL is by dextrose i.v. infusion.

4- Peritoneo-venous shunt (LeVeen shunt) is inserted (in case of failure of diuretic therapy) that routes ascitic fluid subcutaneously from the peritoneal cavity to the internal jugular vein through a one-way valve catheter. This shunt may cause low-grade disseminated intravascular coagulopathy and infection.

5- The TIPS procedure is best used to control ascites.

6- Large volume paracentesis 4-6 liters/day is an alternative to the diuretic therapy in some patients with tense ascites, with simultaneous infusion of i.v. salt-poor albumin (about 10 g/L of ascitic fluid).

7. Central Nervous System:

Hepatic Encephalopathy: occurs in 50-70% of patients.

Clinical Picture:

- There are mental state changes and fluctuating neurological signs such as astrexis (flapping tremors), hyper-reflexia, and inverted planter reflex.
- Electroencephalograph (EEG) changes such as symmetric high voltage slow-wave activity.
- **No cerebral edema** occurs due to presence of compensatory changes against the increased osmotic pressure (**cerebral edema and increased intracranial pressure** with the possibility of herniation occur **only with acute encephalopathy** as in fulminating hepatic failure).

Cause: There is **shunting** of portal blood away from the liver (with liver impairment) directly to the systemic circulation. This allows **substances absorbed from the gastrointestinal tract to bypass metabolism in the liver. Therefore, these substances reach the systemic circulation as ammonia, methionine, metabolites such as mercaptans, short chain fatty acids, and phenols with an increase in**

aromatic amino acids and a decrease in branched chain amino acids. This occurs with increased permeability of blood brain barrier and increased γ- amino-butyric acid in the brain.

Precipitating Factors:

- Gastrointestinal bleeding or increased dietary protein intake.
- Hypovolemia or hypotension.
- Hypokalemic alkalosis (from vomiting or diuresis).
- Infections.
- Bad liver functions.
- Sedatives or opioids.
- Creation of porto-systemic shunt as TIPS procedure.

Preoperative Treatment:

1- Correct precipitating factors.
2- Dietary protein restriction.
3- Non-absorbable disaccharides such as oral lactulose
4- Non-absorbable antibiotics such as neomycin or metronidazole to decrease intestinal ammonia absorption.
5- Avoid premedications in patients with history of encephalopathy because they are sensitive to central nervous depressants.
6- Flumazenil (a benzodiazepines antagonist) is tried.

8. Infections:

- Spontaneous bacterial peritonitis may occur.
- Screening for viral hepatitis is needed.

9. Acute Decompensation:

Acute decompensation may occur in a patient with chronic liver failure due to the same precipitating factors of acute encephalopathy.

Premedications:

1- Sedatives: should be **avoided** in patients with **hepatic encephalopathy.**
2- I.m. injections should be avoided due to coagulopathy (so use oral or i.v. routes).
3- Preoperative management should be continued.

Intraoperative Management

Extra-caution is indicated as **avoiding contact** with blood and body fluids from these patients by gloves, masks, protective eye wear and avoiding recapping needles, and vaccination (against B virus).

Aim:

Preservation of the hepatic arterial perfusion because the liver is dependent mainly on its arterial supply (the portal venous blood is decreased); so, avoid any decrease in the hepatic blood flow.

Monitoring:

Besides the standard monitors,

- Arterial blood gases.
- Invasive arterial blood pressure.
- Central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP).
- Urine output: If urine output is decreased in spite of maintaining fluid replacement, give mannitol and low-dose dopamine.

Avoid unnecessary esophageal instrumentation (esophageal stethoscope, orogastric or nasogastric tube in patients with known esophageal varices).

Choice of Anesthesia:

a- Regional Anesthesia:

It can be used if there is no coagulopathy, or hypotension. Avoid large doses of amide local anesthetics because they are metabolized in the liver and cause toxicity.

b- General Anesthesia: is more preferred.

Generally, the response to anesthetic agents is unpredictable in patients with cirrhosis due to altered protein binding and metabolism.

Induction:

Rapid-sequence induction with cricoid pressure or **awake intubation** is used due to:

- Preoperative nausea and vomiting.

- Upper gastrointestinal bleeding.
- Abdominal distension from massive ascites.

Induction Agents:

- The duration of action of many induction agents is determined initially by redistribution; so, prolongation of action may not become apparent until a subsequent dose has been given.
- Hypotension after induction of anesthesia may occur because of the low systemic vascular resistance and relative hypovolemia that may be present in these patients. This can usually be treated with small amounts of vasoconstrictors (phenylephrine).
- **Thiopentone;**
  - Its clearance is unchanged because its reduced metabolism is balanced by the decrease in protein binding.
  - The central nervous system of cirrhotic patients is sensitive to thiopentone; therefore, the dose of thiopentone should be decreased except in alcoholic patients, the dose should be increased due to presence of cross tolerance.
- **Ketamine** can be used if there is hypotension.
- **Etomidate** is generally safe.
- **Suxamethonium** may show a prolonged action due to decreased pseudo-cholinesterase level. Actually, this has no clinical significance. If the patient has renal failure, care for hyperkalemia should be taken.

Maintenance:

Balanced anesthesia is used with the following precautions:

- **N_2O may be avoided** if the patients have large right to left intra-pulmonary shunts to avoid hypoxia.
- **With the exception of halothane, all volatile anesthetics (in small doses) are suitable** for patients with severe liver diseases. The doses of volatile agents should be decreased to minimum to avoid the persistent decrease in mean arterial blood pressure, which increases postoperative mortality and morbidity.
- **Opioids** should be **used in small doses** to decrease the dose of volatile agents, but they can cause respiratory depression as they are metabolized in the liver (meperidine is better than morphine).
- **Muscle relaxants:**
  - The increased volume of distribution due to expanded extracellular fluid that accompanies cirrhosis, especially with ascites, will result in the need for **a larger initial dose** of non-depolarizing muscle relaxant to produce the required plasma concentration.
  - **Atracurium** is of choice; its metabolite, laudanosine, may accumulate causing convulsions.
  - Muscle relaxants that depend on hepatic metabolism such as pancuronium, or vecuronium require smaller than normal maintenance doses.
- **Controlled ventilation and positive end-expiratory pressure (PEEP)** are used to:
  - avoid hypoxia and
  - maintain normal $PaCO_2$ because hypercapnia decreases hepatic blood flow, and to avoid any increase in intracranial pressure (ICP), if there is encephalopathy.

Intraoperative Fluid Replacement:

Aim: To preserve i.v. volume and urine output to avoid hypotension and renal shutdown.

There are usually great fluid shifts due to:
- venous engorgement from portal hypertension.
- the associated coagulopathy.
- evacuation of ascites.
- prolonged surgery and adhesions from previous surgeries.

Type of Fluids:

1- I.v glucose should be given to **prevent hypoglycemia.**

N.B.: Intraoperative glucose infusion is needed in:
- Pediatric patients.
- Diabetic patients.
- Hepatic patients.
- Hypernatremia.
- Critically-ill patients.
- Any patient with documented hypoglycemia.

2- Colloids are **better** than crystalloids to avoid sodium overload.

3- Red blood cell transfusion is given in anemic patients. Follow the rule of 1 unit transfused for each 1 unit blood loss. **Whole blood is preferred** to packed red cells.

Fresh frozen plasma, cryoprecipitate and platelet transfusion are used to correct coagulation factors and platelet deficiencies respectively.

N.B.: **I.v. Ca^{++}** is often needed to reverse the negative inotropic effect of the decrease in ionized Ca^{++} in blood due to citrate toxicity (because citrate, which is used as anticoagulant in blood units, is not metabolized in cirrhotic liver).

Postoperative Management

- Regardless of the drugs selected for anesthesia, **postoperative liver dysfunction or jaundice** is likely in patients with chronic liver diseases (see before the causes of postoperative liver dysfunction).
- **Manifestations of alcohol withdrawal** usually appear 24 to 72 hours after cessation of drinking and can constitute a medical emergency.

Diseases of the Biliary Tract

Causes: Decreased bile flow causing cholestasis.

1- Extra-hepatic Obstruction of Biliary Tract (Extra-hepatic cholestasis or Obstructive Jaundice) such as gallstone or tumors.

2- Intra-hepatic cholestasis such as drug-induced or infection (figure 22-4).

The causes are discussed above.

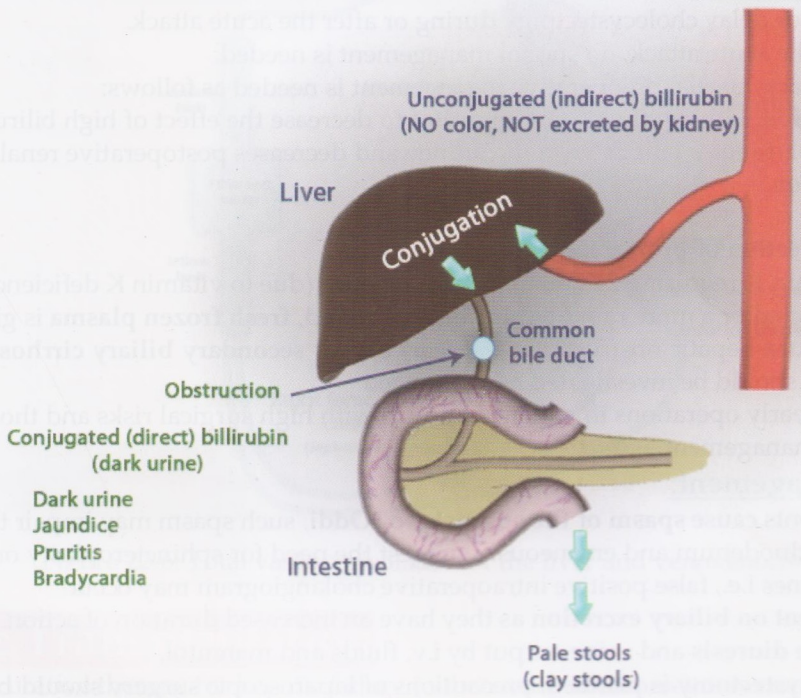


Figure 22-4: Hepato-biliary diseases

Clinical Picture:

- Patients with complete obstruction show progressive jaundice, dark urine, pale stools, and pruritis (figure 22-5).
- Choledocholithiasis (a stone in the common bile duct) causes biliary colic and transient jaundice.
- Cholangitis (ascending infection in biliary system) causes chills and fever.
- Acute pancreatitis occurs, if a gallstone obstructs the pancreatic duct.

Investigations:

- Increased conjugated bilirubin.
- Increased serum alkaline phosphatase (moderate to severe), but a mild increase in amino-transferase.
- Ultrasonography may show a dilated common bile duct.
- Cholangiograms are either:
  - endoscopic retrograde cholangio-pancreatography (ERCP), which is indicated initially to identify the cause and to remove the stone, endoscopic sphincterotomy, or to place a stent, or
  - percutaneous trans-hepatic cholangiography.
- Radio-isotope and CT scans to diagnose extra-hepatic causes.

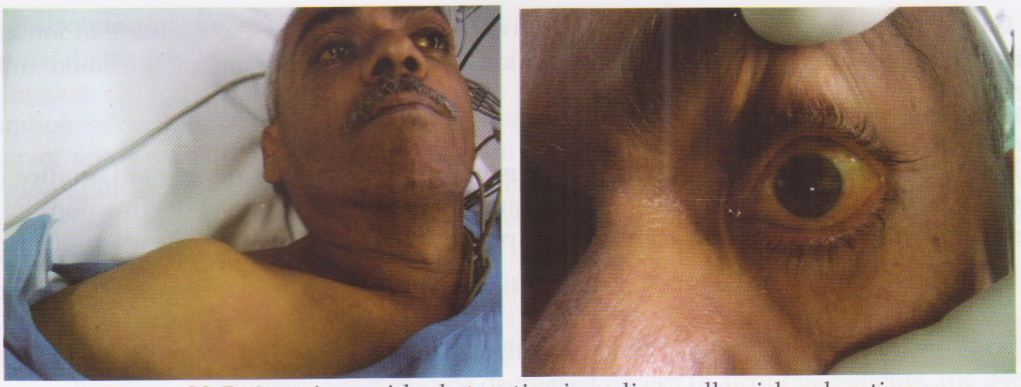


Figure 22-5: A patient with obstructive jaundice; yellowish coloration appears in the skin and conjunctiva

Treatment:

1- ERCP.
2- Operative exploration of the common bile duct is indicated if endoscopy is unsuccessful.

Preoperative Management:

It is a controversy to do or delay cholecystectomy during or after the acute attack.

- After resolution of the acute attack, no special management is needed.
- During the acute attack, special preoperative management is needed as follows:

1- Adequate hydration with i.v. fluids and **mannitol** to decrease the effect of high bilirubin levels on the kidney. Mannitol excretes bilirubin via the kidney and decreases postoperative renal failure.

2- Nasogastric suction.

3- Antibiotics.

4- Preoperative correction of prothrombin time (PT) by:

- **Parenteral vitamin K** requiring 24 hours for full response (due to vitamin K deficiency).
- If PT is not corrected or a more rapid correction is required, **fresh frozen plasma** is given.

5- Long standing extra-hepatic obstruction **(> 1 year)** causes **secondary biliary cirrhosis and portal hypertension.** They should be investigated and managed.

Current practices favor early operations in patients who are with high surgical risks and those who fail to improve with medical management.

Intraoperative Management:

- **Opioids** in some patients cause **spasm of the sphincter of Oddi**; such spasm may impair the passage of contrast media into the duodenum and erroneously suggest the need for sphincteroplasty or the presence of common bile duct stones i.e., false positive intraoperative cholangiogram may occur.
- **Avoid drugs dependent on biliary excretion** as they have an increased duration of action.
- Maintain **preoperative diuresis** and urine output by i.v. fluids and mannitol.
- If **laparoscopic cholecystectomy** is planned, precautions of laparoscopic surgery should be considered. These precautions and anesthetic problems are discussed in chapter "Laparoscopic Surgery".

Hepatic Surgery

There are many types of surgical procedures such as:

- repair of lacerations,
- tumor resection,
- abscess drainage or hydatid cyst excision or
- liver transplantation.

Anesthetic Problems:

All the anesthetic management of liver cirrhosis should be considered if the patient has **a cirrhotic liver**.

1- **Blood loss** is common during liver procedures; therefore, the following precautions should be taken.

- **Multiple large-bore i.v. cannulas** should be inserted.
- **Cell saver devices, rapid infusion devices, and blood warmers** are very helpful.
- **There are surgical maneuvers**, which limit blood loss from the exposed liver parenchyma. These surgical maneuvers include:

a- **Intermittent clamping of the portal tract** with/without supra- and infra-hepatic **inferior vena cava clamping.**

b- **Total vascular isolation of the liver** with **cooling of the liver** and **venovenous bypass.** Heparin-bonded cannulas are used where one cannula is inserted in the portal vein via the inferior mesenteric vein while the other cannula is inserted into the right femoral vein via the saphenous branch and both are connected to the inflow limb of the venovenous bypass. Venous blood is returned to the patient via a cannula inserted in the right axillary vein (figure 22-6).

2- **Hypotensive anesthesia** is contraindicated during hepatic surgery.

3- **N_2O** should be avoided because of ▫ the long period of operations, which results in gut distension.
▫ fear of air embolism during vascular isolation of the liver.

4- **Hypoglycemia** may occur after large liver resection.

5- **Peritoneal contamination** may occur after **abscess drainage**.

6- **Anaphylaxis** may occur after **hydatid cyst drainage** with spillage of echinococcus antigen.

7- **Hypothermia.**

8- **Renal protection** in jaundiced patients (i.v. fluid and mannitol).

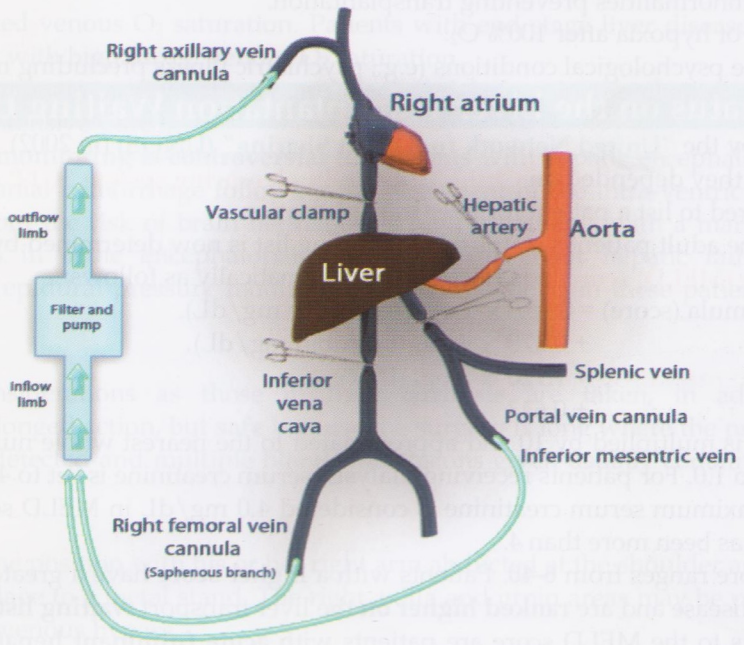


Figure 22-6: Total vascular isolation of the liver and venovenous bypass

Hepatic Transplantation

It is the only curative therapy for hepatic failure (either acute or chronic). It is from either:

- **A Cadaver**: The liver can be split to provide grafts for two recipients (usually one adult and one pediatric patient).
- **A live donor**, but there may a problem of size matching where the small-for-size syndrome may occur and manifests as liver dysfunction within the first week after surgery. It is more common nowadays.

Orthotopic liver transplantation: is the transplantation where the recipient's liver is excised and replaced entirely with a donor liver **in the same anatomic position.**

Hepatic transplantation is a lengthy operation lasting 6-18 hours (average 8 hours). One-year survival rate is > 85% in some centers, while 5 years survival rate is 50-60%.

Indications of Liver Transplantation

1- End-stage liver disease such as causes of liver cirrhosis (mentioned before). Cirrhosis resulting from hepatitis C is the most common indication of liver transplantation in western countries and developing countries as Egypt.

2- Primary liver malignancy (hepatocellular carcinoma of the liver): Those with:

- a single tumor smaller than 5 cm in diameter.
- three or fewer tumors, the largest of which is smaller than 3 cm in diameter.

3- Fulminant acute hepatic necrosis.

4- Biliary atresia (is the most common indication for pediatric liver transplantation).
5- Budd-Chiari syndrome.

N.B.: Hepatic failure after **viral** related infection is **controversial** because:

- there is a high incidence of **re-infection** (near 100%) with hepatitis B and C.
- patients with long standing chronic active hepatitis have a 200-fold increased risk of hepatocellular carcinoma. The susceptibility of malignancy is increased by immuno-suppression.

Absolute Contraindications

1- Positive human immune deficiency virus (HIV) serology.
2- Extra-hepatic malignancy.
3- Cholangio-carcinoma.
4- Active untreated sepsis.
5- Advanced cardio-pulmonary disease.
6- Active alcoholism or substance abuse in the previous 6 months.
7- Anatomic abnormalities preventing transplantation.
8- Persistence of hypoxia after 100% O_2.
9- Unfavorable psychological conditions (e.g., psychiatric illness precluding medication compliance).

Patients' Status on the Liver Transplantation Waiting List

It is organized by the "United Network for Organ Sharing" (UNOS) (in 2002)

- **In the past**, they depended on Child-Turcotte-Pugh scoring system "CTP score" (see before) as score > 7 was required to list a patient for liver transplantation.
- **Recently**, the adult patient's status on the waiting list is now determined by the Model for End-Stage Liver Disease (MELD) score. It is calculated mathematically as follows:
  - MELD formula (score) = 0.957 x Log_e (creatinine mg/dL).
    + 0.378 x Log_e (bilirubin mg/dL).
    + 1.120 x Log_e (INR).
    + 0.643
  - The score is multiplied by 10 and approximated to the nearest whole number. Laboratory values < 1.0 are set to 1.0. For patients receiving dialysis, serum creatinine is set to 4.0 mg/dL and in the same time the maximum serum creatinine is considered 4.0 mg/dL in MELD score equation if the serum creatinine has been more than 4.

  - MELD score ranges from **6-40**. Patients with a **higher score** have a greater short-term risk of dying from liver disease and are **ranked higher on** the liver transport **waiting list**.
  - **Exceptions** to the MELD score are patients with **acute fulminant hepatic failure** who have a life expectancy of < 7 days without a liver transplant. These patients are termed **status 1** and are **ranked highest** on the waiting list. This group with acute fulminant hepatitis includes:
    - Patients without a prior history of liver disease who develop acute hepatic failure.
    - Patients who suffer **primary graft non-function** or **hepatic artery thrombosis within 7 days** of a liver transplant.
    - Patients with **acutely decompensated Wilson's disease.**
- For pediatric patients, Pediatric End-Stage Liver Disease Model (PELD) score is used. It is similar to MELD, but uses bilirubin, INR, and **albumin**, and incorporates the **child's age and growth** failure into the formula.

Anesthetic Management

Preoperative Management

- The same as **preoperative management** as in **liver cirrhosis** (are discussed above in details).
- **Evaluation of anatomic suitability** of liver transplantation as weight, height, and chest measurements should be performed preoperatively.
- Investigations such as magnetic resonant imaging (MRI), duplex, angiography, and ultrasonography are essential.
- Other systems should be assessed to exclude contraindications.
- Methyl prednisolone and azathioprine are given before the surgery.

Intraoperative Management

Monitoring:

In addition to the **monitors discussed above in liver cirrhosis,**

- **Invasive blood pressure** is better performed via **the radial artery** than infra-diaphragmatic sites because the abdominal aorta is occasionally cross-clamped during hepatic arterial anastomosis. **Two lines** are inserted in each arm, one for arterial blood pressure (heparinized), and the other for blood sampling for coagulation study (un-heparinized).
- **Central venous line: is preferred in veins above the diaphragm** over infra-diaphragmatic sites because supra-hepatic inferior vena cava is clamped during the surgery.
- **Serial hematocrit** is needed to guide blood replacement.
- **Thromboelastography** is essential to assess the coagulation status during the procedure.
- **Oximetric thermodilution pulmonary artery catheter** can be used for:
  - Assessment of ventricular function.
  - Measurement of cardiac output by thermodilution method. It may be difficult during liver transplantation if moderate hypothermia develops during the anhepatic phase of the operation. Room temperature injectate is used for measurement of cardiac output to avoid exacerbation of hypothermia.
  - Measurement of mixed venous O_2 saturation. Patients with end stage liver disease have systemic and pulmonary shunts with high mixed venous O_2 saturation.
  - Other values of pulmonary artery catheter are discussed before in the chapter of "Monitoring during Anesthesia & Intensive Care".
- **Intracranial pressure monitoring** is **controversial** for patients with hepatic encephalopathy because there is a risk of intracranial hemorrhage following the placement of the intra-ventricular catheter in coagulopathic patients, but the risk of brain herniation is high in patients with a marked increase in intracranial pressure as in acute encephalopathy in acute fulminant hepatic failure. Therefore, continuous intra-cranial epidural pressure monitoring is recommended in these patients with severe encephalopathy.

Induction:

The same anesthetic considerations as those in **liver cirrhosis** are taken, in addition to that **suxamethonium** has a prolonged action, but **safe** because the surgery is long where the prolonged action of suxamethonium is not detected and multiple blood transfusions given usually contain cholinesterase enzyme.

Patient Position:

The patient lies in the supine position with his or her right arm abducted at the shoulder and flexed at the elbow. It is fixed by a bandage to a metal stand. The right axilla and groin areas may be prepared for the possible institution of venovenous bypass.

Maintenance:

The same anesthetic considerations as those in **liver cirrhosis** are taken in addition to:

- **N_2O is avoided** or used only before perfusion of the donor graft to:
  - avoid marked bowel distension.
  - avoid expansion of venous air embolism if it occurs.
- **Muscle relaxants'** choice is not important because the patients are routinely left intubated at the end of surgery.
- Measures to **avoid hypothermia** should be taken because the operation is long and there is increased blood loss.

Intraoperative Complications

The operation is divided into 3 phases.

I) Pre-anhepatic (Dissection) Phase: (Phase of Native Hepatectomy)

It begins with a **wide subcostal incision**. The liver is dissected so that it remains attached only by the inferior vena cava, portal vein, hepatic artery and the common bile duct. It ends with clamps over these vessels. The anesthetic problems during this phase include:

1. Massive Blood Loss: occurs due to:

- Preoperative coagulopathy and thrombocytopenia.
- Previous abdominal surgeries.
- Increased venous collaterals between the portal and systemic venous circulation.

Therefore,

1. Insert 3-5 large **venous cannulas** (14 or larger gauge). Avoid cannulation in the arm that may be used for venovenous bypass.

2. Prepare **multiple blood transfusions** as these operations typically require
   15-30 units of red blood cells.
   15-30 units of fresh frozen plasma.
   15-30 units of platelets.
   10-20 units of cryoprecipitate.
   Nowadays, fewer blood transfusions are needed.
3. **Fluid (and blood) warming devices** should be available.
4. **Rapid infusion devices** should be available. They need 8.5 F specialized catheters in the antecubital veins. They can infuse up to 2 L/min.
5. **Blood salvaging (saving) devices** should be available. They can decrease the blood needed by 25-30%.
6. **Aprotinin** (*Trasylol*) **or E-amino-caproic acid** infusion.
7. **Correction of coagulopathy** with the help of thromboelastography or standard laboratory tests (prothrombin time, fibrinogen, and platelets transfusion).

2. Renal Protection:

1- Adequate i.v. fluid replacement.
2- Dopamine (dopaminergic dose); just after induction of general anesthesia, but its value is doubtful.
3- Mannitol 20% 1 g/kg i.v. 1 hour before venovenous bypass.
4- Loop diuretics such as furosemide 1 mg/kg i.v. They increase renal blood flow, decrease renal O_2 consumption, and preserve the renal function.

3. Calcium Chloride Infusion:

It is given to correct hypocalcemia, which occurs due to citrate-rich blood transfusion in absence of hepatic function.

4. Vasopressin Infusion:

5-10 U/hour is started before portal decompression with venovenous bypass (if used) to decrease the splanchnic blood flow and the portal hypertension. Vasopressin should be discontinued before reperfusion of the liver.

5. Magnesium Sulfate Infusion:

200 mg/hour are given through the pre-anhepatic, anhepatic, and reperfusion phases to:

- Provide hemodynamic stability.
- Prevent sympathetic induced ventricular arrhythmias especially during the reperfusion phase.
- Correct hypomagnesemia caused by citrate-rich blood transfusion.

II) Anhepatic Phase:

This phase begins with clamping of inferior vena cava, portal vein, hepatic artery, and common bile duct then the liver is excised. Venovenous bypass may be done and the liver is anastomosed. It ends with **vascular anastomosis** and graft reperfusion.

Vascular Anastomosis of Liver Transplantation

There are 3 options of the anastomosis of inferior vena cava (IVC).

a- End-to-end interposition of the donor inferior vena cava (IVC) to the recipient IVC with clamping of IVC: It is the standard method of reconstructing the vascular connections; the supra-hepatic vena cava and the infra-hepatic vena cava are clamped and divided. Blood flow through the IVC is completely interrupted. A cylinder of the recipient's IVC, that is the segment receiving the hepatic veins, is removed *en bloc* with the diseased liver, often with venovenous bypass to support the circulation. The graft supplies a cylinder of IVC to reconstruct the IVC.

b- End-to-end anastomosis of the vena cava to the hepatic veins (the Piggyback method): The diseased liver is dissected off the IVC. The recipient's IVC is thereby preserved and blood flow is not completely interrupted, usually preventing the need for venovenous bypass. One end of the graft's segment of IVC is over sewn, and the open end is anastomosed to the preserved recipient IVC. The anastomosis may be constructed with the stump of the recipient's hepatic veins.

Advantages of the piggyback method (vena cava preservation):

- Hemodynamic stability due to IVC preservation and maintaining of venous return.
- No need for venovenous bypass with its complications.
- A decrease in the possibility of damage to the adrenal vein.

Disadvantage of this technique:

- The possibility of outflow obstruction resulting in hepatic congestion.

c- Side-to-side cavo-cavostomy: A side-to-side cavo-caval anastomosis is created (figure 22-7).

The anastomosis of hepatic arteries of the donor and recipient is performed by direct connection.

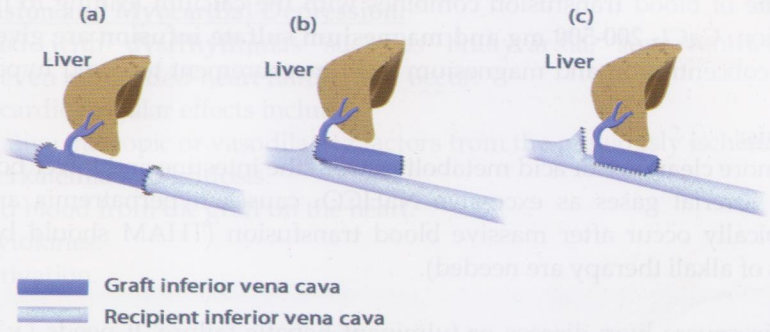


Figure 22-7: IVC connections

The anesthetic problems during this phase include:

1- Hemodynamic Effects of Clamping IVC (Supra- and Infra-Hepatic) and Portal Vein:

On clamping,
- venous return is decreased by about 50% resulting in a decrease in cardiac output and hypotension proximally.
- increased venous pressure occurs resulting in
  - increased bleeding,
  - impaired renal perfusion, and
  - increased edema, splanchnic congestion, and ischemia of the intestine.

N.B.: **Test Clamp Maneuver** is done in supra-hepatic IVC to assess the effect of clamping. If there is severe circulatory depression during the test clamp, the actual clamping of IVC is delayed and reassessment of the volume status, cardiac performance, metabolic state (especially serum Ca^{++}), and the effect of anesthesia is done. If there is still circulatory depression, venovenous bypass is advised.

N.B.: Some patients (usually children) tolerate caval clamping due to extensive trans-diaphragmatic collateral venous channels.

To avoid these problems:

a. Venovenous Bypass (Vascular Isolation of the Liver):

It is not routinely performed at all centers where some centers perform it while other centers never do it. It is done in adults and children > 10 kg body weight.

Vascular isolation of the liver is discussed above where IVC is cannulated (via the saphenous of the right femoral) and portal vein is cannulated (via the inferior mesenteric vein), then diverting their blood flow (1-3 L/min) away from the liver and back to the heart via the right axillary vein. The pump and the tubes usually use heparin bonded circuitry; so, systemic heparinization is not necessary.

Advantages:
- It decompresses splanchnic vessels that promote early return of the gut motility.
- It decompresses renal veins that decrease acute renal dysfunction and improve renal perfusion pressure.
- It improves the heart filling.

Disadvantages (risks of venovenous bypass):
- It increases the operative time.
- It increases the risk of venous air embolism.
- It increases thrombo-embolic complications, but it is decreased if a minimal flow rate (1 L/min) is maintained. Fresh frozen plasma, platelets, and cryoprecipitate should be avoided during the bypass.
- It increases hypothermia (up to 33-34 °C); therefore, it is connected to a heat exchanger to warm the patient during this phase up to 36-37 °C.
- It may produce brachial plexus injury.
- Hemodynamic stability is maintained if venovenous bypass flow rate is > 2 L/min in adults.

b. Temporary Inotropic Support (+ Blood and Fluids): is needed transiently until an effective veno-venous bypass is established.

2- Metabolic Effects of Anhepatic Phase:

Removal of the liver may produce the following metabolic effects:

a- Hypocalcemia (and hypomagnesemia):

Hypocalcemia (and hypomagnesemia) is common due to absence of citrate metabolism (due to liver removal). Citrate of blood transfusion combines with the calcium leading to hypocalcemia and cardiac depression. **$CaCl_2$ 200-500 mg and magnesium sulfate infusion** are given guided by serum ionized Ca^{++} concentration and magnesium level measurement to avoid hypercalcemia or hypermagnesemia.

b- Metabolic Acidosis:

Because there is no more clearance of acid metabolites from the intestine and lower body, $NaHCO_3$ is given guided by arterial gases as excessive $NaHCO_3$ causes hypernatremia and metabolic alkalosis, which typically occur after massive blood transfusion (THAM should be considered when large amounts of alkali therapy are needed).

c- Hypoglycemia:

It occurs especially in severe liver disease or fulminant hepatic failure. It needs i.v. glucose containing solutions.

Hyperglycemia is more common due to the large amounts of transfused blood products. Glucose containing solutions are not used except if hypoglycemia is documented.

d- Reduced drug metabolism during this phase is common.

3- Immuno-Suppressant Therapy:

Immunosuppressant therapy such as **OKT-3** and **azathioprine** are usually given during this phase. Their side effects are discussed in the chapter of "Pharmacological Adjuncts to Anesthesia & Intensive Care ".

III) Post-Anhepatic Phase (Neo-Hepatic Phase) (Reperfusion of the Liver):

In this phase, revascularization (re-assessed by duplex) and biliary reconstruction are established to the new liver. The anesthetic problems during this phase include:

1) Air Embolism:

Air may enter the hepatic sinusoids and may produce pulmonary or systemic paradoxical embolism due to extensive arteriovenous communications. To decrease the incidence of air embolism, the following procedures can be done:

1- **Infusion of cold lactated ringer via the portal vein and hepatic artery of the new liver** should be done while venous anastomoses are being constructed. It also removes solution of University of Wisconsin (containing high potassium ions).

2- After completion of the portal and supra-hepatic caval anastomosis, but before completion of the infra-hepatic caval anastomosis, **the portal vein clamp is released.** Therefore, blood from the portal vein flushes out any air remaining in the liver, which can now escape through the incomplete infra-hepatic caval anastomotic site (marked hypotension may occur needing inotropes and i.v. fluids), after flushing, venous clamps are reapplied until infra-hepatic caval anastomosis is completed (figure 22-8).

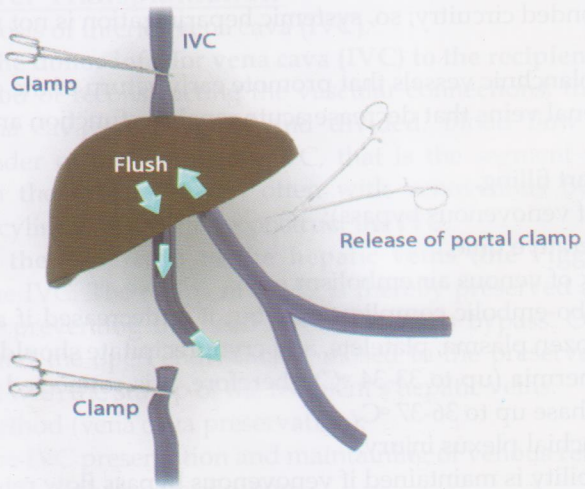


Figure 22-8: Air embolism removal

N.B.: Vasopressin infusions are stopped before the reperfusion.

2) Effects of De-clamping and Reperfusion of Transplanted Liver (Reperfusion Phenomenon or Post-reperfusion Syndrome):

a. Marked Hypotension and Myocardial Depression:

They are associated with **dysrrhythmias** such as bradycardia, supraventricular or ventricular dysrrhythmias and even right sided-heart failure may occur.

The causes of these cardiovascular effects include:

- Washout of negative inotropic or vasodilating factors from the previously ischemic tissues.
- Associated hyperkalemia and acidosis.
- The effect of cold blood from the graft on the heart.
- The release of cytokines.
- Complement activation.

Treatments include:

- Myocardial depression is usually transient. It is treated by $CaCl_2$ 1-4 g i.v. and $NaHCO_3$.
- If persistent, inotropes are given as dopamine or adrenaline. They usually control the arterial blood pressure within 30 min.

N.B.: Do not give i.v. fluids or blood as this causes engorgement of the transplanted liver. If this occurs, nitroglycerin infusion should be used to decompress the engorged liver.

b. Hyperkalemia: Serum K^+ usually increases 1-2 mEq/L due to:

- K^+ release from any remaining preservative solution.
- associated metabolic acidosis.

It is treated by $CaCl_2$ and $NaHCO_3$.

c. Hypernatremia: (usually 150-158 mmol/L)

It can be limited by infusion of hypotonic i.v. fluids after hemodynamic stability.

d. Metabolic Acidosis: occurs due to the release of large acid load from ischemic tissues in the lower body (especially without venovenous bypass). Prophylactic $NaHCO_3$ is usually given.

3) Coagulopathy:

is common during liver transplantation due to:

- Thrombocytopenia.
- Decreased coagulation factor levels.
- Fibrinolysis, which may occur due to an absence of liver produced plasminogen activator inhibitor resulting in *the unopposed action of tissue plasminogen activator.*

Therefore, ▫ Proper coagulation profile and thromboelastography are needed.

▫ *Management of appropriate blood components such as platelets and fresh frozen plasma* units. The hematocrit should be maintained pre-, intra-, and postoperatively between 26-32% by blood transfusion.

▫ Some centers use antifibrinolytics such as amino-caproic acid 1g i.v. to inhibit the plasmin action on fibrin.

4) Continue $CaCl_2$ and Mg SO_4 Infusion.

5) Prostaglandin E_1 Infusion:

It starts at 10 µg/hour and is increased up to 40 µg/hour after hemodynamic stability after reperfusion of the transplanted liver. It increases blood flow to the transplanted liver.

6) Hypothermia:

It is a major problem during reperfusion. The temperature reaches 34-35°C in spite of the active measures taken. It is used as a marker that the cold graft outflow reaches the central circulation.

7) Document Warm and Cold Ischemia Time:

- **Warm ischemia time:**

It is the time from harvesting, in which the vessels of the donor liver are cross-clamped, until perfusion by the cold solution of University of Wisconsin, in addition to the time from the placement of the new liver in the recipient abdomen until its reperfusion. It should be **as short as possible.** Its average is **1-2 hours**. It is the time (1) + (3) as shown in figure 22-9.

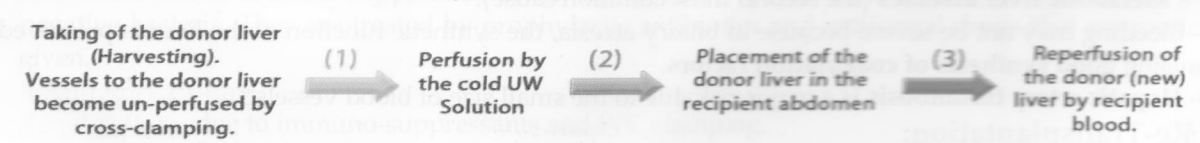


Figure 22-9: The warm and cold ischemia times

• **Cold ischemia time:** It is the time (2).
It is the time from perfusion by solution of University of Wisconsin until placement of the donor liver in the recipient's abdomen. It should be **< 24 hours.**

8) Neo-hepatic Function can be estimated by the following:

1. The Appearance of the Liver should be of good color, not distended, with sharp margin, and soft in substance.

2. Enhanced Production of CO_2 is an early indicator of graft function. This is due to enhanced metabolism of organic acids by the new liver. This is observed by a rise in end-tidal CO_2.

3. Return of Metabolic Functions is indicated by improvement of acidosis and development of **metabolic alkalosis**, but this may not be apparent if there is continuous blood loss after reperfusion of the new liver.

4. Hypokalemia occurs several hours after reperfusion. It may need K^+ supplementation.

5. Normalization of Coagulation Factors is assessed by measuring **prothrombin time (PT), partial thromboplastin time (PTT), platelets, coagulation factors, fibrinogen, V, VII, and VIII** factors (they are **continuously measured** through all phases of surgery). Normalization of coagulation factors takes hours to days after the transplantation to be corrected.
Factor VII has a relatively long half-life 4-7 hours. A rapid increase in factor VII concentration is a good index of hepatic function.

6. Appearance of Bile Production.

7. Measurement of Mono Ethyl Glycine Xyloidide (MEGX): 1 mg/kg xylocaine i.v. is given then MEGX level is determined. If MEGX level is > 100 ng/mL, this indicates a good function.

8. Serum Transaminase and Serum Glucose return to normal.

9. Increased Urine output is a very important indicator.

10. Rising Core Temperature.

11. Decreased Ca^{++} Requirement.

Special Situations during Liver Transplantation

A) Transplantation of Acute Fulminant Hepatic Failure:

The same anesthetic management as liver transplantation, but care is taken for **acute encephalopathy. During acute fulminant hepatic failure,** there is cerebral edema and increased intracranial pressure (ICP) (in up to 80% of patients), which may cause brain herniation. There is a change of the level of consciousness up to coma. Acute hepatic failure needs preoperative intensive care admission.

Therefore, **the following precautions** should be applied:

- Frequent assessment of the mental status.
- Avoidance of sedatives which can obscure the neurological changes.
- Airway management if grade III (stupor) or IV (coma) occurs to avoid aspiration, which can preclude liver transplantation.
- Avoiding the increase in intracranial pressure during intubation as usual.
- Monitoring of ICP. If the ICP is increased > 25 mm Hg, it should be treated.
- Monitoring of cerebral perfusion pressure by trans-cranial Doppler. It should be above 50 mm Hg.

Management of brain protection should be applied such as:

- Decreasing ICP by diuretics, mannitol, elevation of the patient's head 10-20 degrees….etc.
- Maintaining arterial blood pressure.
- Treatment of agitation.

Sustained cerebral hypoperfusion i.e., < 40 mm Hg, is a contra-indication to liver transplantation in many centers.

B) Pediatric Liver Transplantation:

The same anesthetic management as adult liver transplantation, but with the following considerations:

1- The main indications of liver transplantation in pediatric patients include:
- **Biliary atresia** (the most common cause).
- **Metabolic liver diseases** (the second most common cause).

2- Bleeding may not be severe because in biliary atresia, the synthetic function of the liver is preserved causing **good synthesis of coagulation factors.**

3- **Hepatic artery thrombosis** is a major risk due to the small size of blood vessels.

C) Re-Transplantation:

1- Early re-transplantation (within days of the first transplant):

It is due to: ▫ primary non-function of the graft or
▫ surgically uncorrectable portal vein thrombosis.

It is **easier surgically** as the dissection planes are already present, but **difficult medically** as the patient has fulminant hepatic failure.

2- Late re-transplantation (within years of the first transplant):

It is due to chronic rejection.

It is difficult surgically as adhesions are present.

D) Living Donor Transplantation:

It is the most common in many countries and its rate is increasing allover the world.

1- Adult-to-adult transplantation: The right lobe is transplanted.

2- Adult-to-pediatric transplantation: The left lobe is transplanted.

Postoperative Management and Intensive Care Considerations

In **the intensive care unit (ICU)** usually for 7 days for:

1) Ventilatory Support:

Ventilatory support is routine in all patients; therefore, do not reverse muscle relaxants or stop opioids at the end of surgery. Weaning from mechanical ventilators occurs when:

- Coagulopathy is controlled (it may need repeated fresh frozen plasma, platelets, and cryoprecipitate infusion guided by coagulation profile).
- Neo-hepatic function returns to normal.
- Renal function is normal.
- Temperature returns to normal.
- There is no evidence of complications as sepsis or pulmonary congestion.

2) Assessment of Neo-Hepatic Function: (Monitor of the graft function)

As discussed above. Diagnosis of rejection is done by **liver biopsy.**

3) Postoperative Immuno-suppressive Therapy:

such as cyclosporin, corticosteroids, azathioprine, OKT-3, and tacrolimus. They are discussed in more details in chapter "Pharmacological Adjuncts for Anesthesia & Intensive Care".

4) Postoperative Analgesia:

- Patient controlled analgesia, epidural, or paravertebral blocks can be used, but epidural analgesia is rarely used due to coagulopathy.
- Avoid non-steroidal anti-inflammatory drugs as they interact with calcineurin inhibitors (cyclosporin or tacrolimus) and induce renal failure.

5) Postoperative Fluid Management:

- Maintenance fluid/nasogastric feeding at 1.5 mL/kg/hour.
- Blood, colloids, fresh frozen plasma are given to maintain central venous pressure at 10-12 cm H_2O, hematocrit at 26-32%, and PT at < 23 seconds.

6) Postoperative Complications:

1. Primary Non-Function of the Liver:

It occurs in 7-10% of the transplants with mortality of 80% and is presented by:

- Increased serum transaminases.
- Decreased bile production.
- Hypoglycemia.
- Severe coagulopathy.
- Hepatic encephalopathy.
- Metabolic acidosis.
- Acute renal failure.

Treatment:

1- **PGE_1 infusion** (10-40 µg/hour) as long as there is no evidence of hemodynamic instability as it increases the blood flow.

2- **Hepatectomy and re-transplantation** are very difficult because transplantation is not always available.

2. Severe Systemic Infections:

due to the use of immuno-suppressive drugs e.g. candida, epstein barr virus, cytomegalovirus, gram negative bacteria. They are treated by prophylactic antibiotics and antifungal drugs that are routinely given.

3. Respiratory Failure.

4. Renal Failure: due to immuno-suppressants and IVC clamping.

5. Metabolic and Fluid Disturbances: as metabolic alkalosis, hypokalemia, fluid overload, and hyperglycemia.

6. Surgical Complications:

1. Persistent hemorrhage.
2. Bile leak.
3. Stricture or thrombosis of the portal or hepatic vessels.

7. Early Postoperative Death: can occur due to:

- Thrombosis of the graft vessels. It should be monitored by duplex. It requires thrombectomy and if failed, super-urgent re-grafting may be necessary.
- Cholangitis.
- Air embolism.

8. Coagulation Disorders: as disseminated intravascular coagulopathy (DIC) and hyper-fibrinolysis.

N.B.: **Bio-artificial liver support** is being investigated in selected centers as a bridge to transplantation. Most recently, the development of hybrid bio-artificial support systems using hepatocytes from human or xenogenic sources has shown some promise.

Anesthesia for Patients with a Transplanted Liver

Generally, the functioning graft (liver) metabolizes drugs in a normal fashion.

Anesthetic Problems:

1- **Strict sterile techniques** are very important to avoid infection in these immuno-suppressed patients especially if regional anesthesia or invasive monitors are applied.

2- A **stress dose of corticosteroids** is required for patients on chronic steroid therapy.

3- **Immuno-suppressive side effects** should be investigated and managed. For example, renal function should be assessed and managed carefully as cyclosporin is associated with renal impairment. Side effects of immuno-suppressant therapy are discussed in chapter "Pharmacological Adjuncts for Anesthesia & Intensive Care".

4- Normal physiological mechanisms that protect hepatic blood flow are blunted after liver transplantation. The liver is normally an important source of auto-transfusion of blood volume in shock states via a vasoconstrictive response and this mechanism may be impaired after liver transplantation.

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Web Sites:

http://www.ezzatmoemen.com/scoring-system-for-hepatic-dysfunction

ENDOCRINE DISEASES

23

- The pancreas
  - Insulinoma
  - Diabetes mellitus
- The thyroid
  - Hyperthyroidism
  - Hypothyroidism
- The parathyroid
  - Hyperparathyroidism
  - Hypoparathyroidism
- The adrenal
  - Mineralocorticoid excess (Conn's syndrome)
  - Mineralocorticoid deficiency
  - Glucocorticoid excess (Cushing's syndrome)
  - Glucocorticoid deficiency (Addison's syndrome)
  - Acute adrenal insufficiency (Addisonian Crisis)
  - Perioperative and Intensive Care Steroid Cover
  - Catecholamine excess (pheochromocytoma)
- Carcinoid tumor and syndrome
- Apudomas
- The pituitary
  - Pituitary tumors
  - Acromegaly
  - Panhypopituitarism
  - Inappropriate secretion of antidiuretic hormone
  - Diabetes insipidus

Gland	Hormone	Hyper-secretion	Hypo-secretion
1) The pancreas	• Insulin	• Insulinoma	• Diabetes mellitus
2) The thyroid	• Thyroxine	• Hyperthyroidism	• Hypothyroidism
3) The parathyroid	• Parathyroid hormone	• Hyperparathyroidism	• Hypoparathyroidism
4) The adrenal **a- Adrenal cortex** **- Zona glomerulosa**	30 different corticosteroids are secreted. The most important are: • Aldosterone	• Mineralocorticoid excess (Conn's syndrome)	• Mineralocorticoid deficiency.
- Zona fasciculate	• Cortisol	• Glucocorticoid excess (Cushing's syndrome)	• Glucocorticoid deficiency (Addison's syndrome)
- Zona reticularis	• Sex steroids (androgen and estrogen)	They have no effect on anesthesia	
b- Adrenal medulla	• Epinephrine (80%), nor-epinephrine, and dopamine (20%)	• Catecholamine excess (pheochromocytoma)	Not present as a disease
5) The pituitary **a- Anterior pituitary**	• Growth hormone • Corticotropin (adreno-corticotropic hormone "ACTH") • Prolactin	• Acromegaly or gigantism • Cushing's syndrome • Hyper-prolactinemia	• Pan-hypopituitarism (for all hormones) • Monotropic deficiency (for solitary hormone)
b- Posterior pituitary	• Antidiuretic hormone (ADH) • Oxytocin	• Inappropriate secretion of antidiuretic hormone	• Diabetes insipidus
6) Others		• Carcinoid tumor and syndrome • Multiple endocrine neoplasia	

The Pancreas

Adults normally secrete approximately 50 U of insulin every day from the β-cells of the islets of Langerhans in the pancreas.

Endocrinologic Effects of Insulin

a) Effects on the Liver:

1. **Anabolic:** Insulin is the most important anabolic hormone. It stimulates:
   - glycogenesis and glycolysis,
   - synthesis of cholesterol, triglycerides, and very low density lipoproteins (VLDL) and
   - protein synthesis.

2. **Anticatabolic:** Insulin inhibits:
   - glycogenolysis,
   - ketogenesis, and
   - gluconeogenesis.

b) Effects on Muscle:

1. **Insulin stimulates protein synthesis:**
   - It increases amino acids transport.
   - It stimulates ribosomal protein synthesis.
2. **Insulin stimulates glycogen synthesis:**
   - It increases glucose transport.
   - It stimulates glycogen synthetase.
   - It inhibits glycogen phosphorylase.

c) Effects on Fat:

Insulin stimulates triglyceride storage:

- It stimulates lipoprotein lipase increasing free fatty acids which are absorbed into fat cells.
- It increases glucose transport into fat cells, which is used in triglyceride synthesis.
- It inhibits lipolysis.

Insulinoma

It is an insulin-secreting tumor of pancreatic beta cells. It is malignant in 10% of cases sending secondaries to the liver.

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Clinical Picture: Fasting hypoglycemia may cause:

- Hypertension, tachycardia, or diaphoresis (sweating). These symptoms are masked during anesthesia.
- Some patients adapt to blood glucose concentrations as low as 40 mg/dL, whereas others may experience a hypoglycemic reaction when the level is abruptly decreased from 300 mg/dL to 100 mg/dL.

Treatment:

1- Surgical removal.

2- Streptozotocin: inhibits pancreatic beta cells. It is used as a palliative therapy for inoperable metastatic disease.

Anesthetic Management:

The aim is to maintain normal blood glucose level. Blood glucose can change markedly during anesthesia because: ▫ profound hypoglycemia may occur especially during manipulation of the tumor.
▫ profound hyperglycemia may occur especially after successful surgical removal of the tumor.

Control of blood glucose is maintained by:

- A **blood glucose meter** allows frequent (every 15min) measurements of the blood glucose concentrations.
- An **artificial pancreas** continuously analyzes the blood glucose concentrations and automatically infuses insulin or glucose intraoperatively.

Volatile anesthetics are used for maintenance of anesthesia because theoretically they decrease insulin release (not proved clinically).

Diabetes Mellitus (DM)

Diabetes mellitus is characterized by impairment of carbohydrate metabolism caused by an absolute or relative deficiency of insulin or insulin responsiveness, which leads to hyperglycemia and glucosuria.

Classifications:

There is overlapping between the two types:

	Type I (Previously called Insulin Dependent DM "IDDM")	Type II (Previously called Non-Insulin Dependent DM "NIDDM")
Incidence	10% of cases	90% of cases
Possible causes	**Type Ia:** in a genetically susceptible individual who is exposed to an unknown cause, that may be a virus or a drug that causes inflammation of the pancreatic islet cells and lymphatic infiltration with subsequent triggering of the **autoimmune** response leading to destruction of the beta cells. This pathology produces **absolute insulin deficiency** as the amount of insulin is present in very low concentrations. **Type Ib:** is a rare disease with **absolute insulin deficiency**, but it is **not immune mediated.**	Due to a genetic factor with insulin receptor defects **(not immune mediated)** resulting in: • Skeletal muscle and hepatic resistance to the effects of insulin causing normal or high insulin production. • Excessive hepatic glucose release. There is **resistance/relative deficiency of insulin.**
Age	< 16 years (juvenile onset)	> 35 years (maturity onset)
Onset	Abrupt	Gradual
Associated diseases	Type Ia is associated **with** other autoimmune disease e.g., hypothyroidism, graves' disease, myasthenia gravis, and Addison's disease.	It is **not** associated with any autoimmune disease.
Body weight	Lean	Obese
Complications: • **Diabetic ketoacidosis** • **Micro-angiopathy** • **Macro-angiopathy**	• Sensitive to occur • Common • Infrequent	• Resistance to occur • Infrequent • Common
Treatment	Insulin sensitive	Diet, oral hypoglycemic, and insulin.

There are other subtypes of type II:

Maturity Onset Diabetes of the Young (MODY):

It is a heterogeneous group of disorders characterized by non-ketotic diabetes mellitus. It represents 1-5% of all diabetes. It is associated with
- strong family history,
- autosomal dominant inheritance,
- onset before 25 years old,
- symptoms are often present,
- non-obese patients, and
- abnormal beta cell function.

Gestational Diabetes Mellitus:

It is the most common problem during pregnancy. It increases the risk of maternal and neonatal complications. Thirty to fifty % of the pregnant patients develop type II DM later on within 20 years after pregnancy. It needs insulin for its treatment during pregnancy.

Secondary Diabetes Mellitus:

DM may occur secondary to:
- Pancreatic diseases which decrease insulin release.
- Drugs as corticosteroids.
- Endocrine diseases such as Cushing's syndrome, acromegaly, or pheochromocytoma.

Clinical Picture:

Deficiency of insulin causes hyperglycemia and glucosuria. These cause 6 Ps with acute and chronic complications. These 6 Ps include:
- Polyuria.
- Polyphagia (i.e., increased eating) with weight loss.
- Pains and muscle weakness.
- Polydypsia (i.e., increased thirst).
- Pruritis (especially at the vulva and anus).
- Premature loosening of teeth.

Diagnosis: according to the American Diabetes Association.

	Normal values	Prediabetic status	Diabetes mellitus
1- Fasting plasma glucose level	70-100 mg/dL (<5.6 mmol/L) (according to FDA) or 70-110 mg/dL (<6.1 mmol/L) (according to WHO)	100-125 mg/dL (5.6-6.9 mmol/L) (according to FDA) or 110-125 mg/dL (6.1-6.9 mmol/L) (according to WHO)	**>126 mg/dL** (>7.0 mmol/L)
2- Random plasma glucose level	<140 mg/dL	140-199 mg/dL	**≥ 200 mg/dL (>11.1 mmol/L) with symptoms** of diabetes mellitus.
3- Two-hours postprandial plasma glucose level during an oral glucose tolerance test	< 140 mg/dL (7.8 mmol/L)	140-199 mg/dL (7.8-11.1 mmol/L)	**≥200 mg/dL** (11.1 mmol/L)

A prediabetic state means impaired glucose tolerance or impaired fasting glucose.
FDA is Food and Drug Administration WHO is World Health Organization
The above measures depend on plasma glucose level. Blood glucose level is 12-15% lower than plasma glucose level.
N.B.: mg/dL = mg% = mg/100 mL.

4- **Glycosylated-hemoglobin (Glyco-Hb) (HbA_{1c}):**
It is the best measure of overall blood glucose control over the **previous 1-3 months. Normal levels are 4-6%**. Its synthesis depends on non-enzymatic glycosylation of glucose that freely crosses red blood cell membranes.
If the level of glyco-Hb is high e.g., 20%, this indicates poorly controlled diabetes over the previous 1-3 months. Increased risk of microvascular and macrovascular diseases begins at a HbA_{1c} of 6.5% and correlates with increased perioperative risk of morbidity.

N.B.: The Metabolic Syndrome (Insulin-resistant Syndrome):

It is a constellation of clinical and biochemical characteristics frequently seen in patients with or at risk of type II diabetes. At least 3 of the following items should be present:
- Fasting plasma glucose ≥ 110 mg/dL.
- Abdominal obesity (waist girth > 40 inches in men or 35 inches in women).
- Serum triglycerides ≥ 150 mg/dL.
- Serum high-density lipoprotein cholesterol < 40 mg/dL (in men), < 50 mg/dL (in women).
- Blood pressure ≥ 130/85 mm Hg.

The metabolic syndrome combines insulin resistance with hypertension, dyslipidemia, a procoagulant state, and obesity with premature atherosclerosis and subsequent cardiovascular diseases.

Effect of Anesthesia and Surgery on Insulin and Glucose Metabolism:

A) Anesthesia: (alone)

- Halothane, methoxyflurane, thiopentone, or N_2O decrease plasma insulin resulting in an increased glucose level, but they have a very little effect when compared to the stress of surgery.
- Enflurane or spinal anesthesia has no effects.

B) Surgery especially major surgery: (also, shock or sepsis)

- Any stress will stimulate the sympathetic nervous system and activate release of catecholamines, adrenal-corticotropic hormone, cortisol, and growth hormone, which will increase plasma glucose levels i.e., catabolic response during and after surgery and may convert a well-controlled diabetic to one with significant hyperglycemia and even ketoacidosis.

• No effect on insulin level in the plasma, but there is a relative insulin resistant phase after the surgery called insulin resistance of surgery.
Therefore, there is an acute increase in insulin requirement in diabetic patients.

Anesthetic Management:

Preoperative Management:

1) Blood Glucose Level Assessment and Management:

• One third to one half of patients do not know that they are diabetic at the time of surgery.
• Especially for major surgery, if **plasma glucose** is **greater than 270 mg/dL** preoperatively, the surgery should be **delayed** while rapid control is achieved with i.v. insulin. If the plasma glucose is **greater than 400 mg/dL**, the surgery should be **postponed** and the blood glucose level and metabolic state should be re-stabilized (see later).

2) Drug History and Interactions:

The diabetic patients are controlled by either oral hypoglycemic agents or insulin.

a- Oral Hypoglycemic Agents:

Drug Class	Drug Name	Onset	Duration
First generation sulfonylureas	Tolbutamide (*Diamol*)	1 h	12 h
	Acetohexamide	3 h	24 h
	Tolazamide	4 h	16 h
	Chlorpropamide (*Pamidine*)	2 h	24 h
Second generation sulfonylureas	Glyburide	30 min	24 h
	Glipizide IR (*Minidiab, or Glupizide*) (IR= immediate release)	30 min	24 h
	Glipizide ER (ER= extended release)	2-4 h	24 h
	Glimepiride (*Amaryl, Diabeto, Diabenor, Diabride, Dolcyl, Glimadel, or Glimaryl*)	2-3 h	24 h
	Gliclazide (*Diabetron, Diabyl, Diamicron, Dianormal, Glipicrone, Serviclazide,or Unocron*)	2-3h	24 h
	Glibenclamide (*Daonil, Diaben, Euglucon, Euglumide, or Glibenase*)	2-3 h	24 h
Biguanides	Metformin (*Amophage, Cidophage, Diaformin, Diaphage, Glucoformin, or Glucophage*)	1-3 h	17 h
α-Glucosidase inhibitors	Acarbose (*Glucobay*)	2 h	4 h
	Miglitol	2-3 h	Not available
Thiazolidinediones	Pioglitazone (*Diabetin, Ensudyne, Hi Glitazone, or Glustin*)	2 h	Not available
	Rosiglitazone (*Avandia or Rosizone*)		
Amino acid derivative	Nateglinide (*Starlix*)		
Prandial glucose regulator	Repaglinide (*Diarol or Novonorm*)		

b- Insulin Preparations:

Insulin Preparation	Onset	Peak Action	Duration
a- Short acting: • Human regular, Actrapid, Velosulin, Humulin-R	30 min	2-4 h	5-8 h
• Lispro (*Humalog*)	10-15 min	1-2 h	3-6 h
• Aspart (*Novolog*)	10-15 min	1-2 h	3-6 h
• Semi-lente, Semi-tard	30-60 min	4-6 h	12-16 h
b- Intermediate: • Human NPH, Lente, Monotard, Insulatard, Lentard	2-4 h	6-10 h	10-20 h
• Glargine (Lentus)	2-4 h	Peakless; there is a decrease in somogyi events and hypoglycemia	~ 24 h
c- Long acting: • Ultra-Lente, Ultratard, Protamine zinc insulin (PZI)	4-6 h	8-20 h. It has a variable and unpredictable peak	24-48 h

There are inter-individual variations as regard the onset, peak action and the duration.

Drug Interactions

• Thiazides, furosemide, diazoxide, adrenergic drugs (β_2 agonist), corticosteroids, oral contraceptives, and thyroid preparations increase blood glucose level, which causes hyperglycemia.
• Hypotensive drugs such as β-blockers, ganglion blockers, and alcohol decrease blood glucose level, which causes hypoglycemia. These drugs mask the clinical picture of hypoglycemia.
• Oral hypoglycemic agents:
  ▫ Phenylbutazone, dicumarol, and salicylates displace oral hypoglycemics from protein binding.
  ▫ Barbiturates and other sedatives prolong oral hypoglycemics.
  ▫ Phenothiazines and Monoamine oxidaze inhibitors (MAOIs) potentiate oral hypoglycemics

All these drugs increase the effect of oral hypoglycemics resulting in hyperglycemia.
Therefore, **blood glucose monitoring is essential during usage of the above drugs**.

3) Assessment of Complications:

A) Acute Complications:

1- Increased Incidence of Infection (and Delayed Wound Healing):

This is due to a compromised immune system; therefore,
  ▫ strict attention must be paid to aseptic techniques.
  ▫ insulin doses should be increased.

2- Diabetic Ketoacidosis (DKA):

It is more common with **type I diabetes mellitus**, but it may occur *de novo* in a previously undiagnosed diabetic patient.

Causes: • Inadequate insulin dosage.
• Increased insulin requirements.

Precipitating Factors: include infection, trauma, surgical stress, and acute illness such as cerebro-vascular accident, myocardial infarction, or acute pancreatitis.

Clinical Picture: There is hyperglycemia resulting in hyper-osmolarity with over-production of ketone bodies (acetoacetate, β-hydroxybutyrate, and acetone), which causes an early presentation.

• Cardiovascular system: signs of **dehydration and hypovolemia** up to **prerenal failure and shock**.
• Central nervous system: Changes in **sensorium** up to coma (due to cerebral edema).
• Respiratory system: ▫ Dyspnea and tachypnea.
  ▫ **Kussmaul's respiration** i.e., deep and rapid breathing to provide compensatory respiratory alkalosis as a compensation for the metabolic acidosis.
  ▫ **Fruity breath** of acetone.
• Gastrointestinal tract: ▫ More symptoms such as acute abdominal pain, **nausea and vomiting increase the risk of aspiration**.
• Temperature changes: **Hypothermia** due to acidosis and induced peripheral vasodilation.
• Electrolyte deficits: such as hyponatremia, hypokalemia, hypo-phosphatemia, and hypomagnesemia. These ion deficits are to provide electro-neutrality for renal-excreted ketoacids.

The mortality rate is 5-10% due to late complications such as myocardial infarction, infection, and cerebral edema (figure 22-1).

Investigations:
• Arterial blood gases: pH is < 7.25, serum HCO_3^- is < 10 mEq/L.
• Increased ketone bodies (acids) in the blood > 7 mmol/L.
• Increased plasma glucose concentrations.
• Decreased serum Na^+, K^+, phosphate, and Mg^{++}.
• Plasma amylase commonly exceeds 1000 U/L, but does not indicate pancreatitis.

Treatment:
Usually these patients require a nasogastric tube for gastric decompression and bladder catheterization to monitor urinary output.

a. Treatment of Dehydration:
Amounts: **Usually 3 liters** i.v. fluids are required guided by central venous pressure and urine output.
The 1st liter is given in the 1st 30 min.
The 2nd liter is given in the next 1 hour.
The 3rd liter is given in the next 2 hours or at a rate of 200-500 mL/hour.
Types: • **0.9% normal saline** is usually used.
• 0.45% saline is used, if serum Na^+ is > 150 mmol/L (i.e., water loss is > Na^+ loss).

• **Glucose 5%** is added 4-6 hours later, if blood glucose becomes **< 250 mg%** (<15 mmol/L).

Some authors **avoid lactated Ringer's solution** because it is converted to bicarbonate in the liver and may increase serum glucose.

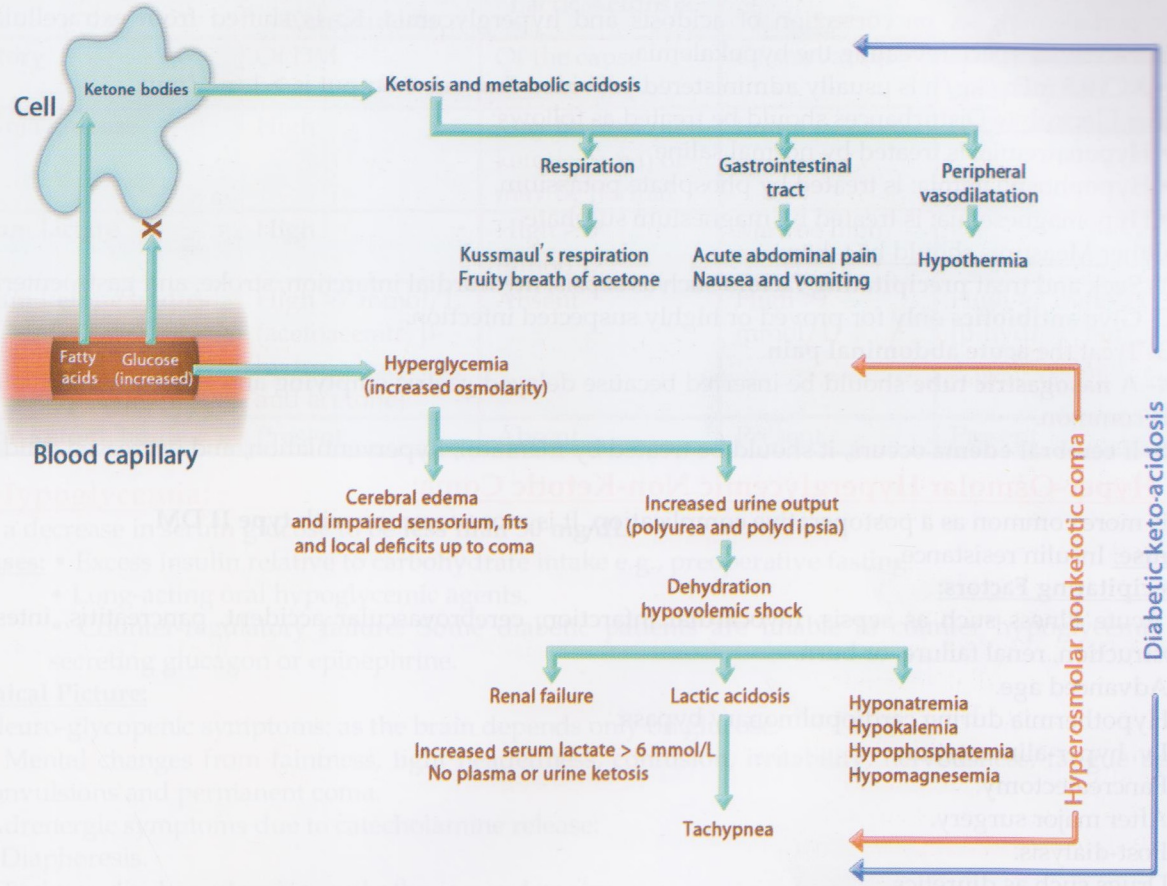


Figure 22-1: Pathophysiology of DKA and non-ketotic coma

b. Treatment of Hyperglycemia:

The aim is to decrease blood glucose level **75-100 mg/dL/h or 10%/h**. This is performed by using **regular crystalline insulin 0.1-0.2 unit/kg i.v.** followed by **0.1-0.2 unit/kg/h i.v. infusion** (or repeated every hour i.m.) monitored by blood glucose and acetone in the urine.

c. Treatment of Acidosis: (high anion gap metabolic acidosis)

Treatment of acidosis is **rarely needed** and is required only if **arterial pH is < 7.2-7.1** because acidosis is usually spontaneously corrected with volume expansion and normalization of the hyperglycemia. $NaHCO_3$ is not routinely given because $NaHCO_3$:

- makes the intracellular acidosis worse,
- causes paradoxical CSF acidosis,
- causes hypokalemia,
- shifts O_2-Hb dissociation curve to the left,
- causes hyper-osmolality, and
- may cause systemic alkalosis (due to over-correction).

$NaHCO_3$ infusion is given as follows:

$$\text{Dose} = \frac{\text{Base deficit}}{2} \times \frac{\text{Body weight}}{3}$$ (i.e., ½ correction) then according to pH monitoring.

d. Treatment of Hypokalemia:

- Hypokalemia is common in DKA, but some patients have hyperkalemia. Hypokalemia occurs due to:
  - vomiting or
  - insulin-glucose therapy.

- Serum potassium should be monitored every 2 hours to avoid hypokalemia (with treatment of acidosis) or hyperkalemia (with potassium administration).
- Some authors recommend that potassium replacement should not be started except **after correction of acidosis** (because acidosis shifts K^+ from intracellular to extracellular space resulting in normo- or hyperkalemia); so, on correction of acidosis and hyperglycemia, K^+ is shifted from extracellular to intracellular space revealing the hypokalemia.
- KCl 0.5 mEq/kg/h is usually administered provided that urine output is > 1 mL/min.

Other Electrolyte Disturbances should be treated as follows:

- Hyponatremia: is treated by normal saline.
- Hypophosphatemia: is treated by phosphate potassium.
- Hypomagnesemia: is treated by magnesium sulphate.

e. Other Measures should be taken:

1- Seek and treat **precipitating factors** such as sepsis, myocardial infarction, stroke, and gastroenteritis.
2- Give **antibiotics** only for proved or highly suspected infection.
3- Treat the **acute abdominal pain**.
4- A **nasogastric tube** should be inserted because delayed gastric emptying and acute gastric dilatation is common.
5- If **cerebral edema** occurs, it should be treated by mannitol, hyperventilation, and decreased fluid rate.

3- Hyper-Osmolar Hyperglycemic Non-Ketotic Coma:

It is more common as a postoperative complication. It is more common with **type II DM**.

Cause: Insulin resistance.

Precipitating Factors:

- Acute illness such as sepsis, myocardial infarction, cerebrovascular accident, pancreatitis, intestinal obstruction, renal failure, or burn.
- Advanced age.
- Hypothermia during cardiopulmonary bypass.
- I.v. hyper-alimentation.
- Pancreatectomy.
- After major surgery.
- Post-dialysis.
- Drugs such as diuretics.

Clinical Picture: **Hyperglycemia** (> 600 mg/dL) causing **hyper-osmolarity** (> 320 mOsm/L) without ketoacidosis, but with lactic acidosis. This causes delayed presentation.

- Cardiovascular system: Osmotic diuresis causes **more dehydration** (7-10 L), **hypovolemia** up to **prerenal failure** and **shock**. There are increased thrombotic events.
- Central nervous system: It is **more** due to changes in the **cerebral** water balance i.e., **brain edema** resulting in mental changes (confusion), fits, and focal deficits as hemiplegia and decreased level of consciousness up to coma.
- Respiratory system: No Kussmaul's respiration or fruity breath as there is no acetone.
- Gastrointestinal tract: No symptoms are present.
- Temperature: There is **low-grade fever** due to lack of acidosis induced peripheral vasodilatation.
- Electrolyte deficits: They are **less severe** because these ions are not required to provide electro-neutrality for renally excreted ketoacids as in DKA.

Investigations:

- Arterial blood gases show acidosis as pH is < 7.25, serum HCO_3^- is < 10 mEq/L. **Lactic acidosis** is present (increased serum lactate > 6 mmol/L).
- No acetone or ketone bodies (acids) in the blood or the urine.
- Increased serum glucose.
- A factitious hyponatremia occurs as each 100 mg/dL increase in plasma glucose lowers plasma sodium concentration by 1.6 mEq/L.

Treatment:

- **Fluid resuscitation** is needed as follows:
  - If the plasma osmolarity is greater than 320 mOsm/L, large volumes (1-1.5 L/h) of **0.45% normal saline** should be administered.
  - If the plasma osmolarity declines to < 320 mOsm/L, large volumes (1-1.5 L/h) of **0.9% normal saline** should be administered.

• **Small doses of insulin and potassium** are usually required (usually less than that of DKA).

Q: What are the differences between diabetic ketoacidosis and non-ketotic coma?

N.B.: Differentiation between different types of acidosis usually mistaken with DKA:

	Diabetic Ketoacidosis	Lactic Acidosis	Starvation Ketosis	Alcoholic Ketosis
History	Of DM	Of the cause	Of starvation	Of alcohol consumption
Plasma glucose	High	May be high (non-ketotic coma) or may be normal	Low	Slightly elevated
Serum lactate	High	High > 6 mmol/L	May be high	-
Serum ketone bodies	High >7 mmol/L (acetoacetate, β-hydroxybutyrate, and acetone)	Absent	High >7 mmol/L	High >7 mmol/L (β-hydroxybutyrate > acetoacetate)
Urine ketone bodies	Present	Absent	Present	Present

4- Hypoglycemia:

It is a decrease in serum glucose to be **less than 50 mg/dL.**

Causes: • Excess insulin relative to carbohydrate intake e.g., preoperative fasting.
• Long-acting oral hypoglycemic agents.
• Counter-regulatory failure: Some diabetic patients are unable to counter hypoglycemia by secreting glucagon or epinephrine.

Clinical Picture:

a- Neuro-glycopenic symptoms: as the brain depends only on glucose.
• Mental changes from faintness, light headedness, confusion, irritability, nervousness, fatigue up to convulsions and permanent coma.

b- Adrenergic symptoms due to catecholamine release:
• Diaphoresis.
• Tachycardia, hypertension, arrhythmias, and angina.

Most clinical pictures are masked by general anesthesia; so, subarachnoid and epidural anesthesia are preferred because regional anesthesia allows early detection of hypoglycemia,
allows early resumption of oral diet postoperatively.

Treatment:

• **Glucose** is given when plasma glucose level is < 100 mg/dL as follows:
▫ Give **dextrose 10 grams (e.g., 20 mL of 50% dextrose) i.v. infusion** (as each 10 gm dextrose bolus increases blood glucose 30-40 mg/dL in a 70 kg adult).
or ▫ **10-20 grams (2-4 teaspoons) of sugar** are given by **mouth or nasogastric tube**.
• Alternatively, give 1 mg of glucagon i.v. or i.m.

B) Chronic Complications:

Many studies have showed that **strict (intensive) glycemic control** (near normal range) **delays the onset** and slows progression **of micro-angiopathic** and micro-vascular complications, **but** this tight glycemic control does **not** affect the progress of the **macro-angiopathy**.

1- Macro-angiopathy: especially in type II DM.

Hypertension, coronary artery disease, peripheral and cerebral vascular diseases are common which should be managed as usual.

For example: • Cardiovascular investigations are essential.
• Careful positioning of the patient in the operating theater if with peripheral vascular diseases and loss of sensation as trivial trauma can cause ulcerations.

2- Micro-angiopathy: especially in type I DM.

a. Nephropathy: may be presented by glomerulosclerosis up to chronic renal failure.

It is detected by proteinuria (albuminuria), which is the earliest laboratory manifestation of diabetic nephropathy followed by increased serum creatinine and blood urea nitrogen within the next 3-5 years. Most patients with type I DM develop chronic renal failure by the age of 30 years. Controlling of

hypertension can markedly slow progression of chronic renal failure. The following measures should be considered: • Avoid nephrotoxic dyes or drugs.
• Maintain adequate hydration.
• Adjust drug doses.
• Low-dose dopamine, mannitol, or diuretics.
• Long-term angiotensin converting enzyme inhibitors (ACE inhibitors) prevent progression to renal failure.

If end-stage renal disease develops, hemodialysis, peritoneal dialysis, continuous ambulatory peritoneal dialysis, and kidney transplantation can be done. A combined kidney/pancreas transplantation results in lower mortality than dialysis or kidney transplantation alone and may prevent recurrence of diabetic nephropathy in the transplanted kidney.

b. Retinopathy:

It is associated with cataract, vitreous hemorrhage, and retinal detachment.

c. Peripheral Neuropathy:

There are two stages of a diabetic peripheral neuropathy:

- **The subclinical stage** that demonstrates laboratory evidence of slowed sensory and motor nerve conduction and elevated sensory perception thresholds in the absence of clinical signs and symptoms.
- **The clinical stage** that demonstrates symptoms and/or neurological deficits. Electro-diagnostic studies of nerve conduction and electromyography define the degree of dysfunction. **A distal symmetrical diffuse sensori-motor polyneuropathy** is the most common form. Sensory deficits usually appear in toes and feet and progress proximally toward the chest in a **"Stocking glove" distribution**. Foot ulcers develop from traumatic events and recurrent infections are common resulting in amputations.

Therefore, ▫ **Avoid local anesthesia** as neurological deficits may be attributed to the local anesthesia.
▫ **Protect pressure points during positioning**, as there is an increased susceptibility to peripheral nerve injury and soft tissue ischemia.

d. Autonomic Neuropathy:

- **Painless (silent) heart ischemia** (detected by ECG).
- Cardiac **arrhythmias** (+ short QT interval).
- **Orthostatic hypotension** and inability of the heart to compensate for intravascular changes causing cardiovascular instability due to sympathetic dysfunction such as after induction of anesthesia (post-induction hypotension) especially if patients are on ACE inhibitors or angiotensin receptor blockers.
- **Resting tachycardia** and absent variation of heart rate with deep breathing due to cardiac vagal denervation.
- **Gastroparesis diabeticorum** causes delayed gastric emptying, vomiting, diarrhea, regurgitation, aspiration, and abdominal distension; so, premedication with **metoclopramide and rapid sequence induction are mandatory.**
- Early satiety.
- Altered regulation of breathing increases **the susceptibility to depressant drugs.**
- Lack of sweating or excessive sweating.
- Neurogenic bladder results in **postoperative urine retention.**
- Impotence.

3- Stiff Joint Syndrome:

Stiff joint syndrome occurs due to non-enzymatic glycosylation of the collagen tissues and proteins (as glyco-Hb). It may affect: ▫ The tempro-mandibular joint causing limited mouth opening.
▫ The atlanto- occipital joint causing limited neck extension.

Both cause difficult laryngoscopy and intubation (30% of type I DM).

Preoperative Investigations:

1- **Diagnosis of diabetes mellitus** as above.

2- **Investigations to detect complications** such as preoperative chest x-ray to detect cardiac enlargement, pulmonary vascular congestion, or pleural effusion, or investigations to detect silent ischemia such as ECG...etc.

Premedications:

1- Antacids and metoclopramide.

2- Short acting oral hypoglycemics can be continued to the day of surgery, but long acting oral hypoglycemics such as sulfonylureas and metformin should be stopped 24-48 hours before surgery.

Intraoperative Management:

Aim:

- **Avoiding hypoglycemia is the primary goal.**
- Avoiding high hyperglycemia (> 250 mg/dL) is the secondary goal.

Therefore, try to maintain serum glucose level between 6-10 mmol/L (110-180 mg/dL).

Tight control of plasma glucose is very important for:

- Patients undergoing **cardiopulmonary bypass** because tight control improves cardiac contractility and allows weaning and decreases infectious and neurological complications.
- **Diabetic pregnant patients** because tight control improves fetal outcome.

Monitoring:

Besides the standard monitors,

- Frequent blood glucose analysis **every 1 h for type I** DM and **every 2-3 h for type II** DM. Blood glucose analysis is best performed by:
  - Portable spectrophotometers (Dextrostix and Ames dextrometer) as a blood drop obtained from a finger stick is exposed to a strip and within 2 min, color conversion of a glucose oxidase impregnated strip occurs which is measured.
  - Obtaining multiple blood samples to be analyzed in the laboratory, but it is time consuming, more expensive, and traumatic to the patient's vein.
- Urine glucose is not accurate for perioperative management.

Perioperative Management of DM:

Many protocols are used, but these protocols are only used as a guide for perioperative glucose control because there are variations between patients and even the need of the patient to insulin may change dramatically. The choice of regimen is dictated by local practice.

A) Alberti's Recommendation:

	Juvenile Onset Diabetes	Maturity Onset Diabetes
Preoperative	1- Check random glucose, urea, and electrolytes. • **In well-controlled patients**: Adjust **insulin**, as soluble insulin subcutaneous bid + **isophane** subcutaneous. • **In poorly controlled patients:** Change **to soluble insulin** subcutaneous tid and delay elective surgery, or give **glucose/insulin infusion** for emergency surgery. 2- On the day of surgery stop all subcutaneous agents and continue with glucose/insulin infusion according to the blood glucose level.	1- Check random glucose, urea, and electrolytes. • **In well-controlled patients**: Change **long** acting oral hypoglycemics (e.g., chlorpropamide) **to short** acting oral hypoglycemics (e.g., glipizide or glibenclamide). • **In poorly controlled patients:** Change **oral** hypoglycemic **to soluble insulin** subcutaneous tid and delay elective surgery, or give **glucose/insulin infusion** for emergency surgery. 2- On the day of surgery (24 h preoperatively) stop all agents and continue with glucose/insulin infusion according to blood glucose level.
Intraoperative Each 1 mmol/L = 18 mg%	Continue **glucose/insulin infusion and K^+ (GIK regimen)** as follows: • Start infusion of **10% glucose (500 mL) + 10 units soluble insulin + 10 mmol KCl** to run **4-6 hourly** on the day of surgery. • Then adjust insulin in the bag according to plasma glucose (i.e., **sliding scale**). < 4 mmol/L..... no insulin is given. 4-6 mmol/L.....5 units insulin/500 mL glucose 10%. 6.1-10 mmol/L.....10 units insulin/500 mL glucose 10%. 10.1-20 mmol/L.....15 units insulin/500 mL glucose 10%. > 20 mmol/L.....20 units insulin/500 mL glucose 10%. • Adjust K^+ dosage according to serum K^+ as follows: < 3 mmol/L.....add 20 mmol KCl on the bag. 3-5 mmol/L.....add 10 mmol KCl on the bag. > 5 mmol/L.....omit KCl. N.B.: Some authors advocate that a sliding scale with short acing subcutaneous insulin for glucose greater than 11.1-13.8 mmol/L (200-250 mg/dL) is ineffective and should not be used.	

Postoperative	1- **Recheck** blood glucose 2-6 hourly and recheck blood urea and electrolytes daily. 2- Continue glucose/insulin infusion. When oral diet is resumed, give soluble insulin subcutaneously tid as the preoperative dosage. Restart the normal regimen when the daily insulin requirements are stable.	1- **Recheck** blood glucose 2-6 hourly and recheck blood urea and electrolytes daily. 2- **In minor surgeries, restart oral hypoglycemics** with the first meal; so, it is better to put the patient the first case on the operation list and just delay the breakfast until recovery from anesthesia. 3- **In major surgeries,** continue **glucose/insulin infusion.** When oral diet is resumed, give soluble insulin subcutaneously 8-12 units tid before each meal. Restart oral hypoglycemic agents when daily insulin requirements are < 20 unit/day

Generally, in 70 kg patient, one unit of regular insulin decreases serum glucose ≃ 25-30 mg/dL (1.5 mmol/L).

B) Bolus Administration Methods:

This method is used if the patient has been on NPH insulin (Neutral Protamine Hagedorn).

Preoperatively:

• Give **½ the morning dose** of NPH insulin (intermediately acting) subcutaneously or intramuscularly. For example, in a patient receiving 30 units NPH, the preoperative dose should be 15 units NPH subcutaneously or intramuscularly.

• 5% dextrose infusion at rate 1.5 mL/kg/h (i.e., about 40 drop/min) is usually added in a peripheral i.v. cannula that is dedicated for 5% glucose.

Intraoperatively and Postoperatively:

• I.v. regular insulin boluses according to the sliding scale are given.

C) Continuous Infusion: (more accurate)

Pre -, Intra - and Postoperatively:

Both regular insulin infusion and glucose infusion are given simultaneously.

• **Regular insulin (short acting) infusion dose** is calculated by either of the following means:

a- Regular insulin units/h = $\frac{\text{Serum glucose (mg/dL)}}{150}$

b- Regular insulin infusion is given according to the sliding scale as follows:

Glucose Concentrations (mmol/L)	Infusion Rate of Insulin (Units/h)
< 4.0	0
4-4.9	0.5
5.0-6.9	1.0
7.0-9.9	2
10-12.9	3
13-15.9	4
> 16	6 (test for ketones)

The regular insulin is administered by a syringe pump as 50 units of human soluble insulin in 50 mL isotonic saline.

Plasma glucose concentration is measured at 1-hourly intervals (initially) and rate of insulin infusion adjusted according to sliding scale. When stability has been achieved, plasma glucose concentration may be measured at 4-hourly intervals. Blood measurements should remain between 6-12 mmol/L.

• **10% dextrose (D_5W) infusion** is administered by another syringe pump to provide adequate carbohydrate and energy without excessive volume. It is given at rate of **100 mL/h**; this provides 240 g of glucose (1000 kcal) in 24 hours.

10 mmol/KCL is added to each 500 mL dextrose because glucose/insulin infusion shifts potassium from extracellular to intracellular spaces.

Insulin and glucose infusions are usually administered by two separate syringe pumps through two separate infusion lines, but some physicians administer both the insulin and glucose in one line because if the i.v. line is malfunctioning, the patient will not receive insulin or glucose alone.

General Precautions during Perioperative Management of Plasma Glucose:

- The effect of **insulin absorption by i.v. tubing** can be minimized by flushing the line before beginning the infusion and it is better to use a glass bottle (if available) to decrease absorption of insulin by a plastic i.v. bag.
- The previous **doses** need to be **increased in stress**, sepsis, hypothermia as there is increase in counter-regulatory hormones (catecholamines, glucocorticoids, growth hormone, and glucagon) leading to relative insulin resistance.
- Patients controlled on diet may develop **starvation ketosis** on the morning of surgery, resulting in presence of acetone in the urine without glucose. It is treated with i.v glucose.
- **Allergic reactions** can occur with insulin up to anaphylactic shock.
  Nonhuman insulin is more allergic than human insulin.
  NPH or protamine zinc insulin is more allergic than protamine sulfate insulin.
- Blood transfusion (with increased citrate concentration) and ringer's lactated (Hartmann's) solutions stimulate gluconeogenesis which increases blood glucose (as lactate is converted to glucose). Therefore, insulin requirements are increased with blood transfusion and ringer lactated solutions, which should be avoided.
- Patient's with **subcutaneous insulin pumps** can either have the pump discontinued and started as an insulin infusion or have the pump placed on a basal rate. In both, dextrose infusion and frequent (every 1-2 hours) blood glucose monitoring are needed.

Postoperative Management:

1- Continue Controlling and Monitoring Blood Glucose Concentration:

This is performed by one of the previous protocols as before. Recent studies show that the **tightly controlled diabetic patients (maintained between 80-110 mg/dL) have less complications**, intensive care unit admission, and mortality than the conventionally treated patients where their serum glucose is maintained between 180-200 mg/dL. The tight controlled blood glucose is beneficial due to:

- Maintenance of macrophage and neutrophil functions.
- Insulin induced beneficial trophic changes on mucosal and skin barriers.
- Enhanced erythropoiesis or decreased hemolysis.
- Decreased cholestasis.
- Anabolic effects of insulin on respiratory muscles and less hyperglycemic injury of neuronal axons. This causes improved liberation from mechanical ventilation.
- Less axonal dysfunction and degeneration associated with hyperglycemia and insulin deficiency.

2- Postoperative Complications:

All the acute complications can occur postoperatively especially:

- Increased incidence of infection.
- Delayed wound healing.
- Hyper-osmolar hyperglycemic non-ketotic coma.

Pancreatic Transplantation

Types of Pancreatic Transplantation:

1- Whole Organ Transplantation:

Whole pancreas transplantation can be done by one of the following methods:

- Simultaneous pancreas and kidney transplant.
- Pancreas transplant after successful kidney transplant.
- Pancreas transplant alone.
- Multi-visceral transplant (pancreas transplant with liver and sometimes small bowel transplant).

The majority of cases receive a pancreas allograft during or after kidney transplantation to prevent recurrence of diabetic nephropathy as well as some of the other microvascular complications.
The recipient's native pancreas and kidney are left in place with placement of the new transplanted organ(s).

2- Segmental Pancreatic Transplantation:

A segment of the pancreas (i.e., the pancreatic tail) is transplanted. It is applicable to live donation.

3- Pancreatic Islet Transplantation:

It is transplantation of the required cell type only (i.e., transplantation of islet cells only) where these cells are isolated by cell-separation techniques and then infused into the portal vein. The islet cells seed the patient's liver and remain viable for more than a year. Islet cells have become fully functional and restore insulin independence or allow the insulin requirement to be decreased, but not eliminated.

Indication of Pancreatic Transplantation:

Pancreas transplantation should be considered as therapy only in diabetic patients who exhibit one of these criteria:

- A history of **frequent, acute, and severe metabolic complications** (hypoglycemia, hyperglycemia, ketoacidosis) requiring medical attention.
- Clinical and **emotional problems** with exogenous insulin therapy that are so severe as to be incapacitating.
- Consistent failure of insulin-based management **to prevent acute complications.**

Pancreas transplantation is associated with the following benefits:

- Reduction of morbidity associated with labile glucose concentrations.
- Stabilization and improvement of secondary diabetic complications.
- Improving the quality of life of patients with diabetes mellitus by restoring normal glucose metabolism.

Contraindications of Pancreas Transplantation:

1- Presence of a recent malignancy.
2- Severe cardiovascular disease.
3- Chronic active hepatitis and/or cirrhosis.
4- Morbid obesity.
5- Older than 60 years.
6- Active alcoholism and/or drug dependency.
7- Smoking.
8- Psychiatric disease.

Criteria of the Donor:

The donor should be:

- younger than 55 years as the cells of the pancreas start to decrease in mass after this age, and
- not obese.

Anesthetic Management:

Preoperative Management:

1- Assessment of other system (by history, examination, and investigations) is important such as:

- detection of silent ischemia,
- detection of left ventricular dysfunction….etc.

Each medical problem should be managed.

2- Metabolic studies such as:

- Glucose tolerance test,
- Glycosylated hemoglobin, and
- Insulin and islet cell antibodies.

Blood glucose level should be tightly controlled.

3- Ultrasonography of the gallbladder is conducted to detect cholelithiasis.

4- Bowel preparation is needed.

5- Broad spectrum antibiotic is required especially i.v. imipenem or cephazolin.

6- Immunosuppressive therapy starts preoperatively such as OKT3, tacrolimus, cyclosporin, prednisone, and mycophenolate mofetil. Side effects of these drugs should be revised.

Intraoperative Management:

- Besides the anesthetic problems of other organ transplantation, which may be transplanted with the pancreas, the blood glucose level should be measured and corrected every 1 h tightly by regular insulin.
- The whole pancreatic transplant should drain its exocrine secretions either into the urinary bladder or the intestine.

a- Bladder drainage:

Advantages: This technique allows allograft exocrine function to be closely monitored (via urine pH and amylase level), which in turn deteriorates during episodes of rejection (urine pH may become acidotic reflecting a decrease in pancreatic bicarbonate secretion and urinary amylase may diminish).

Disadvantages: Bladder drainage results in:

- Irritation of the bladder and urethra leading to infections, bleeding, and strictures.
- Severe metabolic acidosis.
- Reflux pancreatitis.

b- Enteric drainage:

Advantage: It is a more physiological method as it eliminates hyper-insulinemia.

Disadvantage: The enteric drainage procedure has a higher technical failure rate.

Postoperative Management:

Patients are **monitored** in **intensive care unit** with nasogastric tube and urinary catheter to detect the postoperative complications such as:

1- **Causes of post-transplant pancreatic dysfunction:**

a- Mechanical causes:
- Pancreatic duct obstruction.
- Bladder outlet obstruction.
- Bladder or duodenal graft leak.
- Reflux of urine and pancreatic secretions into pancreatic duct.
- Urinary tract infection.
- Thrombosis (venous or arterial).

b- Non-mechanical causes:
- Rejection.
- Immunosuppressive side effects.
- Volume depletion.
- Pancreatitis (bacterial, viral, or fungal).

2- **Rejection.**

3- Complications due to arterial connection; **vascular spasm or thrombosis.** They are the most common cause of graft loss in the first 24 hours detected by a sudden rise in blood glucose and **duplex ultrasound, CT scan, or magnetic resonance imaging**. **Duplex ultrasonography** is routinely performed in the first postoperative days and as needed afterward to assess flow and function in allograft. Measures to **prevent vascular thrombosis of allograft** include:

- Oral aspirin 80 mg/day along with 3000-5000 units of i.v. heparin during the surgery.
- Subcutaneous dalteparin and low molecular weight dextran may be also used.

4- Complications due to **venous connection; hemorrhage**.

5- Complications due to lumen connection; **an anastomotic leak after bladder or enteric drainage**. Pancreatic transplants with bladder drainage result in loss of 1-2 liters of secretions high in bicarbonate and electrolyte content, which requires **supplemental i.v. fluid and bicarbonate replacement** at about 150 mL/h with D_5/half normal saline with 20 mmol/L $NaHCO_3$. **Serum and urinary amylase levels** should be closely monitored and **serum electrolytes** are assessed 3 times daily in the first 48 hours and replaced accordingly. Some patients with urinary bladder-drained pancreatic graft may suffer from **chronic dysuria** because of the presence of amylase in the urine.

6- **Wound infections** due to the immunosuppression.

7- **Hyper-insulinemia** seen after transplant that is due to:

- Diminished insulin clearance by the liver.
- Immunosuppressive drugs such as steroids.
- Denervation of the transplanted pancreas.
- Insulin resistance.

8- Metabolic complications:

- **Metabolic parameters** should be assessed such as fasting serum insulin, lipid profile, and glucagon. Proinsulin to insulin ratios may be used to determine a failing pancreatic allograft.
- **Oral pancreatic enzymes** may be used for malabsorption in the initial postoperative period.
- **Tight control of serum glucose** by insulin infusion is recommended, which becomes unnecessary with commencement of oral feeding (unless the function of the allograft is lost). An acute rise in serum glucose levels or persistently elevated levels above 200 mg/dL requires prompt evaluation with duplex ultrasonography to assess allograft perfusion and function.

The Thyroid Gland

The thyroid is composed of numerous follicles filled with colloid (mainly thyroglobulin). The wall of each follicle is composed of cuboidal cells. Twenty to 40 follicles form a lobule, and lobules form the two lobes and the isthmus of thyroid gland. There are also parafollicular C cells, which produce calcitonin.

Thyroid Hormone Synthesis:

The steps of synthesis are shown in figure 23-2:

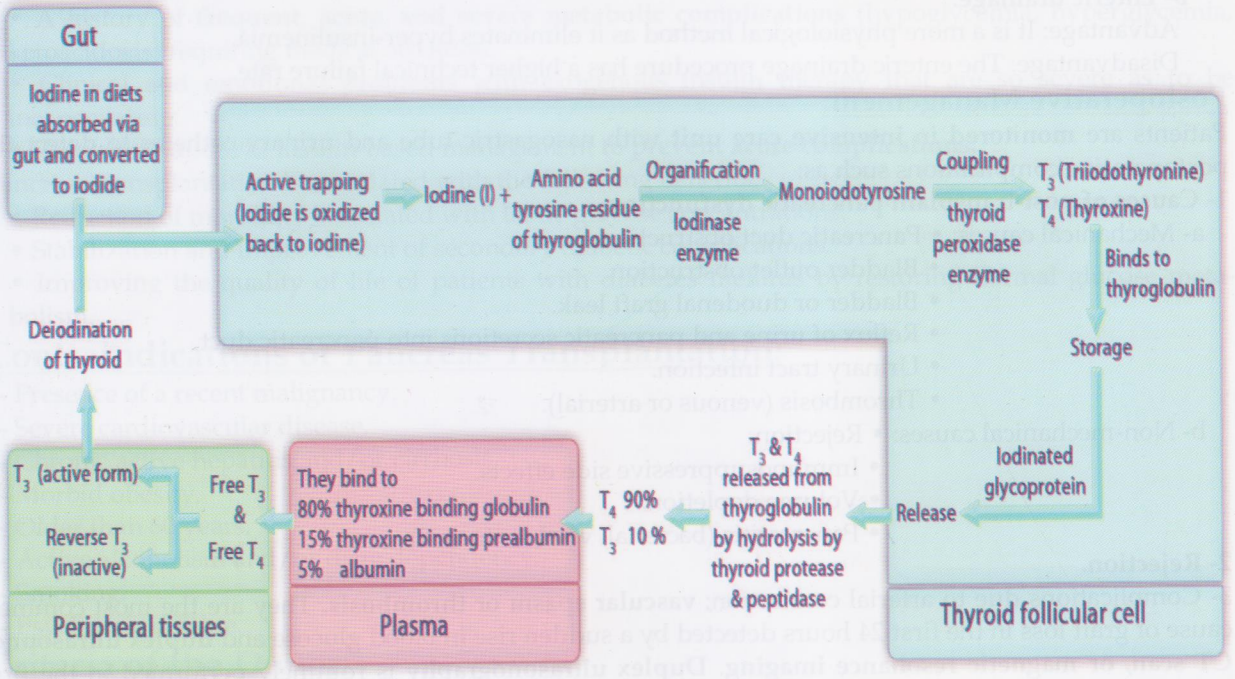


Figure 23-2: Synthesis of thyroid hormone

Hypothalamus secretes thyrotropin-releasing hormone (TRH), which controls the anterior pituitary. The latter secretes thyroid-stimulating hormone (TSH), which controls the thyroid gland (increasing T_3 and T_4).

Function of Thyroid Hormone:

a) Cellular Effects:

- Thyroid hormones **regulate** the nuclear **transcription of messenger RNA in all cells**. T_3 initiates the transcription of biochemical enzymes, which **regulate tissue metabolism**. Basal metabolic rates increase as much as 60% to 100% when large quantities of thyroid hormones are secreted. One of these enzymes that are transcribed in response to thyroid hormone stimulation is Na-K-ATPase.
- Thyroid hormones **regulate cellular energy utilization. They stimulate cellular glucose utilization** by increasing glucose absorption from the gastrointestinal tract, glycogenolysis, gluconeogenesis, insulin secretion, and cellular uptake of glucose. Thyroid hormones increase free fatty acids by increasing lipid mobilization from adipocytes, but they decrease plasma levels of cholesterol, phospholipids, and triglycerides by increasing the rate of cholesterol secretion into the bile.

b) Organ Effects:

- They have a direct effect on the heart as they **increase the heart rate and contractility and decrease systemic vascular resistance via direct vasodilatation, which increase cardiac output.**
- They **increase O_2 consumption and CO_2 production** causing a compensatory increase in respiratory rate and tidal volume.
- They **increase bone formation and catabolism**. This causes changes in parathyroid hormone level.

c) Systemic Effects:

- They increase cellular metabolism increasing the production of metabolic end-products. This causes vasodilatation which increases tissue blood flow.

Thyroid Function Tests:

	Total T_4	Resin T_3 uptake (R T_3U)	Free T_3 index	Free T_4	T_3	Reverse T_3 (r T3)	TSH
1. Euthyroid	N (5-12 µg/dL)	N (24-39%)	N 1.2-4.9	N 0.9-2.4 ng/dL	N 70-195 ng/dL	N	N 0.4-5.0 mIU/L
2. Hyperthyroid	↑	↑	↑	↑	↑	↑	↓ 1ry ↑ 2ry
3. Primary hypothyroid	↓	↓	↓	↓	N, ↓	↓	↑
4. Secondary hypothyroid	↓	↓	↓	↓	N, ↓	↓	↓
5. Thyroxine binding globulin (TBG) excess	↑	↓	N	N	↑	↑	N
6. Thyroxine binding globulin (TBG) deficiency	↓	↑	N	N, ↓	↓	↓	N
7. Non-thyroid illness (Sick Euthyroid syndrome)	N, ↓	↑	N, ↓	↑,N, ↓	↓	↑	N,↓
8. Familial dys-albuminemic hyper-thyroxinemia	↑	N	↑	N	N	N	N

Subclinical Conditions:

- A low TSH level with normal levels of free T_3 and Free T_4 is diagnostic of subclinical hyperthyroidism and usually needs no treatment.
- A low TSH level with elevated levels of free T_3 and free T_4 is diagnostic of overt hyperthyroidism.
- A high TSH level with normal levels of free T_3 and Free T_4 is diagnostic of subclinical hypothyroidism.
- A high TSH level with normal levels of free T_3 and Free T_4 is diagnostic of overt hypothyroidism.

Thyroxine Binding Globulin (TBG) Excess: such as:

- During pregnancy.
- Oral contraceptive pills.
- Infectious hepatitis.
- Newborns.
- Acute intermittent porphyria.
- Drugs as heroin, methadone, clofibrate, and estrogens.
- Familial disorders.

Thyroxine Binding Globulin (TBG) Deficiency such as low protein states e.g.,

- Malnutrition.
- Nephrotic syndrome.
- Cirrhosis.
- Cushing's syndrome.
- Acromegaly.
- Drugs as androgens, anabolic steroids, or glucocorticoids.
- Familial disorders.

Non-thyroid Illness (Sick Euthyroid Syndrome):

A number of non-thyroid illnesses produce alterations in thyroid function (low T_3, low T_3 and T_4, or low TSH syndromes with high reverse T_3 level) in patients in whom no intrinsic thyroid disease is present and the patient is to be euthyroid.

The sick euthyroid syndrome must be distinguished from hypothyroidism because their treatment requires correction of the underlying disorder rather than thyroid hormone replacement.

The sick euthyroid syndrome is essentially a laboratory diagnosis. Patients are clinically euthyroid, but because they have acute or chronic non-thyroid illness, the underlying disease may make assessment of thyroid status difficult or unclear.

Disorders associated with altered thyroid function tests include:

- Acquired immune deficiency syndrome (AIDS)
- Diabetes mellitus.
- Infection.
- Acute myocardial infarction.
- Malnutrition.
- Medications:
  - TSH suppression: dopamine, glucocorticoids, bromocriptine, apomorphine, or octreotide.
  - Impaired thyroid hormone production or secretion: propylthiouracil, methimazole, carbimazole, lithium, iodide, or amiodarone.
  - Impaired T_3 to T_4 conversion: propylthiouracil, glucocorticoids, propranolol, ipodate sodium, or amiodarone.
  - Increased hepatic uptake and metabolism of T_4: phenobarbitone, phenytoin, carbamazepine, or rifampin.
  - Impaired protein binding: salicylates or phenytoin.
- Renal disease.
- Chronic liver disease.
- Cancer.
- Surgery.

Treatment:

- Supportive measures such as adequate nutrition.
- Treatment of the cause in non-thyroid illness.
- Replacement with T_3 in not beneficial.

N.B.:

- **In hypothyroidism (primary or secondary):** T_3 may be normal due to peripheral conversion of T_4 to T_3.
- **Resin T_3 uptake test:** Labeled T_4 or labeled T_3 is injected into the patient then the serum which is enriched with labeled T_4 or T_3 is incubated with a resin that binds the free-labeled T_4 or T_3. In the patient, labeled T_3 will bind to unoccupied hormone binding sites. If these sites are already occupied by endogenous thyroid hormones e.g., hyperthyroid state, labeled T_3 will be picked up by the resin in a greater amount.

T_3 uptake will also be increased when thyroid binding sites are decreased e.g., TBG deficiency.

T_3 uptake will also be decreased in hypothyroidism or in case of increased TBG sites.

Other Thyroid Investigations:

In addition to the **thyroid function tests** and **investigations of other systems to detect complications:**

1- Thyroid Scan: demonstrates iodide-concentrating capacity of thyroid gland; functioning thyroid gland tissues are rarely malignant. Patchy hot spots usually indicate toxic multi-nodular goiter while a single hot spot usually indicates a toxic single adenoma.

2- Ultrasonography: discriminates between cystic (rarely malignant) and solid (may be malignant) nodule.

3- Antibodies to thyroid gland components: discriminate between Hashimoto's thyroiditis from cancer.

4- Chest x-ray to detect retrosternal goiter (figure 23-3).

5- CT scan (figure 23-4).

6- Needle biopsy to exclude malignancy.

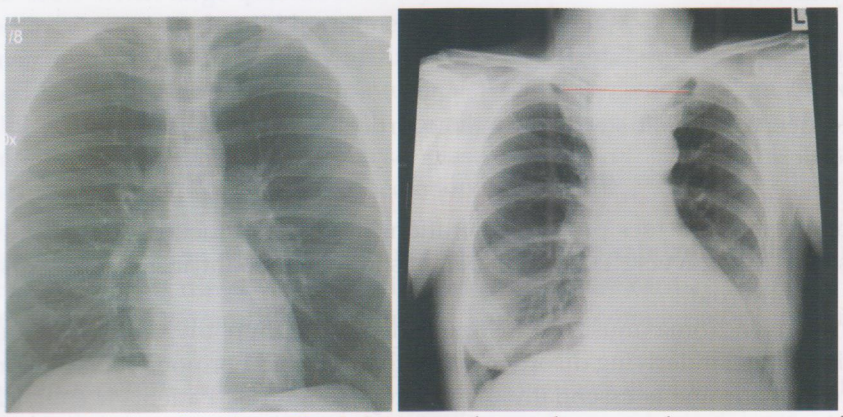


Figure 23-3: Plain chest x-ray PA view. The left image shows the normal appearance of the superior mediastinum on the normal chest x-ray while the right image shows widening of the superior mediastinum continuous with a lower neck shadow likely representing a retrosternal goiter.

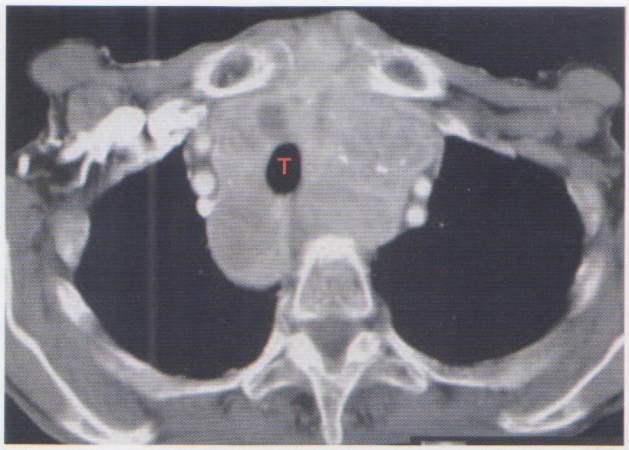
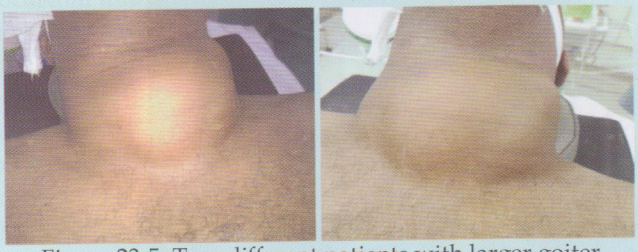


Figure 23-4: CT chest. The thyroid gland is considerably enlarged with retrosternal extension and deviation of the trachea to the right (T)

	Hyperthyroidism (Thyrotoxicosis)	Hypothyroidism (Myxedema)
Causes	**a- Primary Hyperthyroidism:** 1. **Grave's disease** (90%): It is an autoimmune disease where immunoglobulin G (IgG) acts as a TSH-like substance that stimulates the thyroid gland causing thyroid hormone secretion. 2. **Toxic multi-nodular** goiter. 3. **Toxic** (functioning) single **nodule** (adenoma). These three causes represent 99% of cases of thyrotoxicosis. 4. **Over-dosage** of thyroid hormone replacement (accidental or intentional). 5. **Other causes:** • **Struma ovarii**, which is the presence of thyroid tissue in overian teratoma. • Human chorionic gonadotropin-secreting **hydatidiform mole**. • The administration of **iodinated contrast dye** to a susceptible patient. • **Amiodarone**, which can cause hyper-or hypothyroidism. **b- Secondary Hyperthyroidism:** **TSH-secreting pituitary tumors**.	**a- Primary Hypothyroidism:** (95%) 1. Thyroid **gland destruction**: • Chronic autoimmune thyroiditis (**Hashimoto's thyroiditis**) ± other autoimmune diseases e.g., myasthenia gravis, or adrenal insufficiency. • Previous **subtotal thyroidectomy**. • Previous **radio-active iodine** therapy • **Irradiation** of the neck. 2. Thyroid hormone deficiency • **Antithyroid drugs**. • **Excess iodine** decreases thyroid release. • **Dietary iodine deficiency** decreases its synthesis. **b- Secondary Hypothyroidism:** 1. **Hypothalamic dysfunction** causes thyrotropin releasing hormone deficiency. 2. **Anterior pituitary dysfunction** causes thyroid stimulating hormone deficiency.
Clinical Picture	• **Weight loss** (with increased appetite). • **Muscle fatigue and weakness.** • **Diarrhea.** • **Heat intolerance.** • **Hyperactive** reflexes, nervousness, fine tremors, and insomnia. • Cardiovascular system: ▫ Sinus tachycardia up to atrial fibrillation. ▫ Increased cardiac output, which causes hyper-dynamic circulation. This causes high cardiac output heart failure (it is resistant to digitalis). ▫ Warm sweaty extremities. • **Hyperglycemia.** • **Goiter (enlarged gland)** (figure 23-5), which: ▫ compresses the **airway** causing respiratory obstruction. ▫ compresses the **esophagus** resulting in dysphagia. ▫ compresses the **recurrent laryngeal nerve** causing vocal cord paralysis. ▫ compresses the **superior vena cava** (by retrosternal goiter) resulting in superior vena cava syndrome, which	• **Weight gain and a large tongue**. • **Muscle fatigue and weakness.** • **Constipation.** • **Cold intolerance.** • **Hypoactive** reflexes, depression, and dull facial expressions. • Cardiovascular system: ▫ Sinus bradycardia and arrhythmias. ▫ Decreased cardiac output and cardiomyopathy causing congestive heart failure. ▫ Cold mottled extremities (due to peripheral vasoconstriction). • **Hypoglycemia.** • **Goiter:** A goiter results from compensatory hypertrophy and hyperplasia secondary to a reduction in thyroid hormone output. N.B.: A goiter may be associated

	leads to edema and dilatation of the collateral veins of upper thorax, face, neck and upper limb with headache and vertigo.  Figure 23-5: Two different patients with larger goiter • **Exophthalmos** (due to edema and inflammation); when it is severe it is called malignant Exophthalmos. • **With/without other autoimmune diseases** e.g., adrenal insufficiency, myasthenia gravis, and inappropriate secretion of antidiuretic hormone. • **Thyroid Storm (Crisis):** Cause: **Sudden (acute)** release of thyroid hormones into the circulation (not due to the absolute high levels of thyroid hormone). Precipitating Factors: ▫ Thyroid surgery. ▫ Vigorous thyroid manipulations. ▫ Withdrawal of antithyroid drug therapy. ▫ Radioiodine therapy. ▫ Drugs as iodinated contrast dyes, aspirin, or amiodarone. ▫ Non-thyroid illness as, non-thyroid surgery, infection, cerebrovascular accident, congestive heart failure, pulmonary embolism, pregnancy, labor, trauma, and diabetic ketoacidosis. Clinical Picture: They usually occur 6-24 h postoperatively with: ▫ Severe muscle weakness. ▫ Hyperthermia. ▫ Altered consciousness, agitation, delirium, and coma. ▫ Tachycardia, **hypotension**, and congestive heart failure. ▫ Dehydration. Differentiation between thyrotoxicosis and thyroid storm is done by **clinical scoring system** (see later). Differential Diagnosis: ▫ Malignant hyperthermia. ▫ Pheochromocytoma. ▫ Carcinoid crisis.	with euthyroid state, hyperthyroidism, or hypothyroidism. • Pleural and pericardial **effusion.** • **With/without other autoimmune diseases** e.g., adrenal insufficiency, myasthenia gravis, and inappropriate secretion of antidiuretic hormone. N.B.: If hypothyroidism occurs early in life, mental and physical retardation occur and this is called **cretinism**). • Myxedema Coma: Cause: Extreme hypothyroidism. Precipitating Factors: ▫ Surgery. ▫ Infection. ▫ Trauma. ▫ Exposure to cold especially in the elderly. ▫ Myocardial infarction. ▫ Cerebrovascular stroke. ▫ Central nervous system depressant drugs. Clinical Picture: ▫ Severe muscle weakness. ▫ Hypothermia (< 35°C). ▫ Impaired mentation, delirium, up to unconsciousness (which is rare). ▫ Congestive heart failure. ▫ Hyponatremia due to inappropriate secretion of antidiuretic hormone. ▫ Hypoventilation. ▫ Hypotension and bradycardia.
Investigation	Abnormal thyroid function tests (see above).	Abnormal thyroid function tests (see above).
Treatment	**A) Treatment of Thyrotoxicosis:** 1. Drugs inhibiting hormone synthesis: **propylthiouracil** *(Thyrocil)*, **methimazole (*Tapazole*) and carbimazole** *(Carbimazole, Neomercazol)*. 2. Drugs preventing hormone release (in 24 hours) and decreasing vascularity of the gland (in 10 days): **K^+ or Na^+ iodide. Large doses of** Na^+ or K^+ iodide produce a paradoxical effect called the **Wolff-Chaikoff effect**. Rather than catalyze additional incorporation of iodide into thyroglobulin, as might be expected, large doses of iodide suppress gene transcription of thyroid peroxidase (coupling), further reducing the gland's capacity to produce and release hormone.	**A) Treatment of Myxedema:** **Thyroid hormone (L-thyroxine)** *(Eltroxin)* orally: start with 50µg/day then increase the dose up to 150-200 µg/day over several weeks. It needs several days (10-12 days) to produce a physiological effect and several weeks to evoke obvious clinical improvement. **B) Treatment of Myxedematous Coma:** 1- **Thyroid hormone** is given either: • **L-thyroxine** i.v. with loading dose:

	3. Drugs masking signs of adrenergic overactivity: **propranolol** (also it inhibits peripheral conversion of T_4 to T_3). 4. Drugs destroying thyroid cell function: **radioactive iodine; it has replaced subtotal thyroidectomy in some patients.** 5. Surgery: Sub-total thyroidectomy. **B) Treatment of Thyroid Storm**: (aggressive treatment and monitoring). • **Hydration** and treatment of precipitating factors. • **Cooling** by cold fluids, cold lavage of body cavities, cooling blankets, ice packs, low ambient temperature (avoid aspirin as it displaces T_4 from its protein binding sites increasing free T_4. Use paracetamol instead). • **Propylthiouracil** 250 mg/6 hours orally or via naso-gastric tube or rectally. • **Na^+ or K^+ iodide** 1 gm. i.v is given after propylthiouracil by at least I hour and administered over 12 hours then given orally. It also blocks thyroxine synthesis. • **Propranolol** (*Inderal*) 0.5 mg i.v increments until the heart rate becomes < 100/min. • **Cortisol** (100-200 mg/8 h i.v.) or **dexamethasone** (2 mg/6 h i.v.) is used to treat the relative adrenal insufficiency that results from accelerated metabolism. Dexamethasone also inhibits peripheral conversion of T_4 to T_3.	300-**500 µg** of levo-thyroxine in patients without heart disease and maintenance dose of **50-200 µg infusion /day**. It can be given also 0.1-0.2 mg orally or rectally. **L-thyroxine** is contraindicated in elderly patients and those with ischemic heart disease. Or • **L-tri-iodo-thyronine 25-50 µg** bolus followed by infusion. It has a more rapid onset. ECG monitoring is essential. 2- **Hydrocortisone** 100 mg/8 h i.v. (if associated with coexisting adrenal gland suppression, which is a common sequela of hypothyroidism). 3- **Digitalis for congestive heart failure**, but it is usually not given because the hypothyroid heart cannot easily perform increased myocardial contractility power. 4- **Ventilatory support** may be needed. 5- **Hydration** with dextrose 5% and correction of electrolytes. 6- **Correction of hypothermia**. 7- **Treatment of bradycardia.**
Anesthetic Problems	1- Anesthetic problems can be detected from the clinical picture e.g., excessive anxiety, which necessitate sedation. 2- Patient preparation. 3- Patient position. 4- Intraoperative complications. 5- Postoperative complications.	1- Anesthetic problems can be detected from the clinical picture e.g., excessive sedation, which necessitate avoiding preoperative sedation. 2- Patient preparation. 3- Reduced drug metabolism. 4- Delayed recovery.
Preoperative management	**1- Make the Patient Euthyroid:** **a) Elective Surgeries:** (including sub-total thyroidectomy). **Postpone surgery** until the patient becomes euthyroid by one of the following approaches: Slow Approach (requires **6 – 8 weeks**). This delay in effect is secondary to the large store of hormones existing in the gland prior to initiating therapy. Slow approach is by: 1- Antithyroid drugs either: • **Propylthiouracil 100 mg**/8 h orally then decrease the dose after 6 weeks when euthyroid status is reached to 50 mg/8 h orally for another 6-12 months. Or • **Carbimazole 20 mg**/8 h orally then decrease the dose after 6 weeks when euthyroid status is reached to 10 mg/6 h orally for another 6-12 months. 2- **K^+ iodide**, which should follow the antithyroid drugs. K^+ iodide tablet **60 mg/8 h** is given for 10 days to decrease gland vascularity (if euthyroid state is not reached 1st, K^+ iodide will act as a substrate for synthesis of a new thyroid hormone). Rapid Approach (**within 2 weeks**). 1- β-blockers: • **Propranolol 160-480 mg/day** tablets (40-120 mg/6 h) for 2 weeks preoperatively and then followed by **7-10 days postoperatively** (it is given every 6 h due to increased metabolism). Or • **Nadolol** (*Corgard*) (long acting) **160 mg once / day.** 2- **Lugol's iodine** (iodine 5% in 10% K^+ iodide) 10 drops orally/6-8 h for 14 days.	**1) Make the Patient Euthyroid:** Ideally, patients should be euthyroid, but mild to moderate hypothyroidism is not an absolute contraindication for elective surgery as there is no increased risk or perioperative morbidity or mortality e.g., hypothyroid patients with symptomatic coronary arterial disease may benefit from delaying the thyroid therapy until after cardiac surgery. **a) Elective Surgeries:** **Postponed** if the patient has severe hypothyroidism or has myxedematous coma. Preoperative **thyroid hormone** is taken orally until euthyroid state is reached and should be **continued until the morning of surgery**. **b) Emergency Surgeries:** Preoperative thyroid hormone is taken i.v. (as before); see treatment of myxedematous coma.

	Or K^+ iodide tablets 60 mg/8 h. 3- **An antithyroid drug** such as propylthiouracil or methimazole should be administered even though it has a limited effect if taken for less than 2 weeks. **b) Emergency Surgeries:** (within 1 hour). There is an increased risk of postoperative thyroid crisis. • **Propranolol** i.v. (1/10 of the oral dose). • **Esmolol** 100 – 300 µg/kg/min (it does not prevent peripheral conversion of T_4 to T_3). • K^+ iodide 1 gm i.v. or oral 5 drops/6 h. • Hydrocortisone 100 mg/6 h i.v. or dexamethasone 2 mg/6 h i.v. (to prevent peripheral conversion of T_4 to T_3). **N.B.: Treatment of Hyperthyroidism during Pregnancy** 1- **Low doses of antithyroid drugs** can be used. 2- **A subtotal thyroidectomy** can be done. Avoid the following therapies: • Large doses of antithyroid drugs as they cross the placenta and produce fetal goiter hypothyroidism. • Radioactive iodine. • Oral iodide therapy as it can cross the placenta and cause fetal goiter and hypothyroidism. • Long term use of propranolol as it may cause intrauterine growth retardation. **Assess patient's euthyroid state by:** ▫ Thyroid function tests. ▫ Disappearance of the clinical picture e.g., tremors and anxiety. ▫ Resting heart rate < 85 beat/min. **2- Assess Airway by:** Preoperative indirect laryngoscopy to assess vocal cords. Preoperative x-ray neck, CT scan and flow volume loop analysis to assess airway obstruction (see chapter Respiratory Disease). **3- Assess Coexisting Heart Diseases.** **4- Premedication:** • **Sedatives: increase the dose** because: ▫ There is increased anxiety. ▫ There are increased distribution and metabolism. e.g.: - Oral diazepam 10-20 mg. - Oral clonidine 3-5 µg/kg. • **Anticholinergics: should be avoided** because ▫ There is tachycardia. ▫ They interfere with the body's normal heat regulatory mechanisms. • **Antithyroid drugs and β-blockers** should be continued until the **morning of surgery and postoperatively**.	**Assess patient's euthyroid state by:** ▫ Thyroid function tests especially TSH. ▫ Disappearance of the clinical picture **2- Assess Airway:** Large tongue may cause difficult airway management. **3) Assess Coexisting Heart Diseases.** **4) Premedication:** • **Sedatives: avoid or decrease the dose** because ▫ Patients are calm. ▫ There are decreased distribution and metabolism. ▫ To avoid respiratory depression. • **Anticholinergics:** are recommended because: ▫ There is bradycardia. • **Thyroid hormone:** should be continued until the **morning of surgery**. • **Metoclopramide and H_2 blockers** to guard against aspiration.
Intra-operative management **Choice of anesthesia**	**Monitoring:** besides the standard monitors, • Cardiovascular monitors are used according to the patient's condition. • Body temperature. **A) Regional Anesthesia:** • Good sedation is needed. • It blocks the associated increased sympathetic activity provided that local anesthetic solutions **do not contain adrenaline**. **B) General Anesthesia:** **Induction:** • **Avoid the pressor response** of intubation such as by lidocaine or inderal (see chapter of Airway Management) • **Thiopentone** is of choice because of its thiourea structure which has antithyroid action and decreases the peripheral	**Monitoring:** besides the standard monitors, • Cardiovascular monitors are used according to the patient's condition. • Body temperature. **A) Regional Anesthesia:** • **Proper i.v. fluid** replacement is needed. • **Decrease the dose of local anesthetics** especially **amide type** due to the decreased metabolism, which increases the risk of toxicity. **B) General Anesthesia:** **Induction:** • Ketamine (of choice) because

	conversion of T_4 to T_3, but this effect is apparent only at high doses (not the usual doses). • **Ketamine is avoided** because it stimulates sympathetic system, which increases heart rate and blood pressure). **Intubation:** • Use a **smaller sized armored** endotracheal tube because goiter may cause tracheal compression. The endotracheal tube should be placed beyond the thyroid gland in the trachea to avoid the tracheal compression during surgery. • Either **awake or inhalational induction** is used if airway obstruction is suspected. **Maintenance:** O_2/ N_2O + a volatile agent + an opioid + a muscle relaxant. • **Volatile agents:** **Isoflurane, sevoflurane, or desflurane is of choice** because: ▫ It offsets the adverse sympathetic response to surgery. ▫ It does not sensitize the heart to catecholamines. There is **more risk of hepatotoxicity** (of halothane) and **nephrotoxicity** (of enflurane and sevoflurane) due to increased drug metabolism. Although clinical impression shows that **increased MAC** is needed (but not proved by controlled studies) due to: ▫ Increased drug metabolism. ▫ Increased cardiac output that causes an increase in drug uptake, which decreases the alveolar partial pressure; so increasing the inspired concentration of the volatile agents is needed. ▫ Increased body temperature: as increasing the MAC 5% for each degree above 37°C should be done. • **Muscle relaxants:** are used **cautiously** due to the increased incidence of myopathies and myasthenia gravis; so, decrease the initial dose and use a peripheral nerve stimulator. **Pancuronium is avoided** as it stimulates the sympathetic system increasing heart rate and arterial blood pressure. Use **glycopyrrolate (instead of atropine)** to reverse the muscle relaxant. **Intraoperative Problems:** 1- **Intraoperative hyperthermia:** Methods to **decrease the body temperature** such as cooling mattress and cold i.v. fluids are needed. 2- **Intraoperative hypotension:** It is treated by direct sympathomimetics e.g., phenylephrine or epinephrine (avoid indirect sympathomimetics e.g., ephedrine as they increase catecholamines in the hyperthyroid patient who has an increased response to catecholamines). 3- **Intraoperative hypertension:** should be treated. 4- **Intraoperative tachycardia and arrhythmias**: are treated by propranolol i.v. or esmolol infusion. 5- **Intraoperative thyroid storm** (see before). 6- Increased risk of **corneal abrasion** due to exophthalmos; so, the eyes should be protected. 7- **Venous air embolism** in thyroidectomy as the head is usually elevated 15-20 degrees to aid venous drainage and decrease blood loss. **Extubation:** • **Deep** extubation is performed to allow assessment of the vocal cords and airway by direct laryngoscopy or fiberoptic bronchoscopy. • If tracheal collapse is present: ▫ reinsert the endotracheal tube and ▫ tracheostomy set should be available.	hypothyroid patients are more susceptible to the hypotensive effects of other anesthetic agents due to: ▫ The decreased cardiac output. ▫ The blunted baroreceptor reflex. ▫ The decreased intravascular volume. **Intubation:** It may be difficult due to the large tongue. **Maintenance:** O_2/N_2O + short acting opioid or benzodiazepines, or ketamine + a muscle relaxant • **Volatile agents:** They **are avoided** because they produce severe cardiac depression and severe hypotension due to the associated vasodilation and blunted baroreceptor reflex. Although clinical impression shows that **decreased MAC** is needed (but actually does not occur) due to: ▫ Decreased drug metabolism. ▫ Decreased cardiac output that causes a decrease in drug uptake from the alveoli, which increases alveolar partial pressure resulting in rapid induction. ▫ Decreased body temperature, which requires less MAC. • **Muscle relaxants:** are used **cautiously** due to the increased incidence of myopathies and myasthenia gravis; so, decrease the initial dose and use a peripheral nerve stimulator. **Pancuronium: is recommended**. **Use atropine** (instead of glycopyrrolate to reverse the muscle relaxant). **Intraoperative Problems:** 1- **Intraoperative hypothermia:** Methods to **increase body temperature** such as warming mattress and warm i.v. fluids are needed. 2- **Intraoperative hypotension**: It is treated by i.v. fluids and sympathomimetics e.g., ephedrine (avoid phenylephrine, which is an α agonist causing severe vasoconstriction and increasing the afterload on the heart. This results in congestive heart failure). **Refractory hypotension** may be due to: ▫ Coexisting primary adrenal insufficiency. ▫ Presence of congestive heart failure. 3- **Intraoperative hypoglycemia**. **Extubation:** Awake extubation is recommended.

Post-operative management *Q: What are the causes of postoperative respiratory distress in hyperthyroidism?*	Removal of the thyrotoxic gland does not mean immediate resolution of thyrotoxicosis. **The $t_{1/2}$ of T_4 is 7-8 days and $T_{1/2}$ of T_3 is 3 days**; therefore, **β-blockers** may need to be **continued in the postoperative period** while antithyroid drug therapy may be discontinued. **Postoperative Complications:** 1- **Thyroid storm (crisis):** It occurs most commonly 6-24 h postoperatively. 2- **Recurrent hyperthyroidism or iatrogenic hypothyroidism.** 3- Surgical complications: **a. Recurrent laryngeal nerve palsy:** It is usually due to surgical edema (temporary) or surgical trauma (permanent). It either; • affects the abductor fibers (more common) where the affected vocal cord will assume a median or paramedian position. ▫ If unilateral, hoarseness of voice occurs. ▫ If bilateral, aphonia, and stridor on inspiration occur, but no airway obstruction. • affects the adductor fibers (rare). This increases pulmonary aspiration. Therefore, assess the vocal cords by asking the patient to say "e" or by laryngoscopy immediately after deep extubation. Failure of one or both cords to move may require re-intubation and exploration of the wound. **b. Superior laryngeal nerve injury:** causes hoarseness and loss of sensation above the vocal cords thus making patients vulnerable to inhalation of any material present in the pharynx. N.B: The superior laryngeal nerves provide the motor supply to cricothyroid muscles and sensation above the level of the vocal cords. The recurrent laryngeal nerves supply motor innervations to all muscles of the larynx (except the cricothyroid muscle), plus sensation below the level of the vocal cords. **c. Hematoma formation:** It may compress the airway (with normal vocal cords). Therefore, this needs immediate wound exploration and clot evacuation. **d. Tracheomalacia:** due to weakening of the tracheal rings by chronic pressure from the goiter; so, on removal of the goiter, collapse of the trachea occurs. **e. Pneumothorax:** It causes respiratory distress, if surgical dissection is carried down to the mediastinum. **f. Hypo-parathyroidism:** due to interrupted blood supply of parathyroid gland or unintentional removal of the parathyroid glands. This causes acute hypocalcemia within 24-72 h. When serum Ca^{++} becomes < 7 mg%, tetany occurs (with inspiratory stridor, and laryngospasm, anxiety, circumoral numbness, muscle cramping). It is treated by Ca^{++} gluconate 10% 10-30 mL slowly then oral Ca^{++} therapy and vitamin D_3.	**Postoperative Complications:** 1- **Delayed recovery** may occur due to ▫ Slow drug metabolism. ▫ Hypothermia. ▫ Respiratory depression, which needs mechanical ventilation. 2- **Postoperative analgesia** is better by non-steroidal anti-inflammatory drugs or paracetamol. Avoid opioids due to their marked respiratory depression.

Clinical Scoring System to differentiate between Thyrotoxicosis and Thyroid Storm

System	Parameter	Scoring	Maximum points
Thermo-regulatory	Temperature (°F above 98.9)	5 points for temperature of 99-99.9 °F 5 points more for every degree higher up to temperature ≥ 104 °F	30
Central Nervous	Altered mental status	10 points for agitation 20 points for delirium 30 points for seizures or coma	30
Gastro-intestinal	Nausea, vomiting, abdominal pain, hepatic disease	10 points for symptoms 20 points for jaundice	20
Cardio-vascular	Congestive heart failure	5 points for pedal edema 5 points for bi-basilar rales 5 points for pulmonary edema	15
	Rhythm	5 points for heart rate 90-109 beat/min 5 points more every 10 beats/min up to heart rate ≥140 beat/min 10 points for atrial fibrillation	35

The points are summed, and a total of 45 or above is considered suggestive of thyroid storm, whereas a score between 25 and 44 indicates impending storm. Below 25 is only thyrotoxicosis.

The Parathyroid Gland

There are 4 parathyroid glands located behind the upper and lower poles of the thyroid gland and produce parathormone (PTH).

Hypocalcemia stimulates the release of parathyroid hormone (PTH). This increases serum Ca^{++} to normal.

Hypercalcemia inhibits the release of PTH. This decreases serum Ca^{++} to normal.

In other words, PTH maintains normal serum Ca^{++} level by affecting Ca^{++} movement via gastrointestinal system, kidneys, and bones.

	Hyperparathyroidism	Hypoparathyroidism
Causes	**1- Primary hyperparathyroidism:** (serum Ca^{++} is increased). • Adenoma (90% of cases) (figure 23-6). • Hyperplasia. • Carcinoma. **2- Secondary hyperparathyroidism:** (serum Ca^{++} is normal). • Adaptive response to hypocalcemia produced by: ▫ Renal failure. ▫ Intestinal malabsorption syndrome. **3- Ectopic (pseudo) hyperparathyroidism:** PTH-like substances are released from carcinoma of the liver, lung, breast, and pancreas. **N.B.: Other Causes of Hypercalcemia:** 1) Bone secondaries. 2) Vitamin D toxicity. 3) Sarcoidosis or tuberculosis. 4) Prolonged immobilization. 5) Milk-alkali syndrome. 6) Malignancy and chronic inflammation. N.B.: **Hypercalcemic crisis:** may occur especially in elderly with a malignant disease. It is treated by methods, which decrease serum calcium or even surgically (see later).	**1- Decreased or absent PTH.** • Accidental removal during thyroidectomy. • Parathyroidectomy to treat hyperplasia. • Idiopathic (**Di George syndrome**): It is a congenital thymic and parathyroid hypoplasia). **2- Resistance to PTH**: (although PTH is normal) • Congenital pseudo-hypoparathyroidism where the kidneys do not respond to PTH. • Acquired: ▫ Hypomagnesemia and hyperphosphatemia. ▫ Chronic renal failure. ▫ Malabsorption vitamin D deficiency. ▫ Chronic use of phenytoin. • Idiopathic during: ▫ Osteoblastic secondaries. ▫ Acute pancreatitis. **N.B.: Other Causes of Hypocalcemia:** = The same causes of resistance to PTH.
Clinical Picture	**Clinical Picture due to Hypercalcemia:** **1- Central nervous:** personality and mental changes (reduced pain sensation, delirium, psychosis, somnolence, and coma). **2- Cardiovascular:** • Hypertension and ventricular arrhythmias • ECG changes (prolonged PR interval and shortened QT interval). • Cardiac conduction disturbance (when serum Ca^{++} is > 4 mmol/L). **3- Ophthalmic:** • Calcification (band keratopathy). • Conjunctivitis. **4- Musculoskeletal:** • Muscle weakness especially in lower limbs. • Osteoporosis and ostitis fibrosa cystica resulting in pathological fractures. **5- Renal:** • Impaired renal concentrating ability resulting in polyuria, polydipsia, and dehydration. • Hyperchloremic metabolic acidosis. • Renal stones. • Renal impairment up to renal failure. **6- Gastrointestinal:** • Ileus, nausea, vomiting, increased gastric acid secretions (resulting in peptic ulcers) and pancreatitis. **7- Hematopoietic:** anemia.	**Clinical Picture due to Hypocalcemia:** **a. Acute Hypocalcemia:** **Central nervous:** • Laryngospasm, inspiratory stridor, seizures, and tetany. • **Chvostek's sign:** painful twitching of facial muscles after tapping over the facial nerve. • **Trousseau's sign:** Carpopedal spasm after tourniquet inflation above systolic blood pressure for 3 min. • Perioral parasthesia. **b. Chronic Hypocalcemia:** **1- Central nervous:** Mental changes as dementia, depression, and psychosis. **2- Cardiovascular:** • Hypotension and congestive heart failure. • ECG changes (prolonged QT interval, but normal PR interval). **3- Ophthalmic:** Cataract. **4- Musculoskeletal:** • Neuromuscular irritability, twitches, muscle cramps, and weakness.

Anesthetic Problems	1- Anesthetic problems are detected from the clinical picture. 2- Serum Ca^{++} should be decreased (see later).	1- Anesthetic problems are detected from the clinical picture. 2- Serum Ca^{++} should be increased (see later).
Preoperative Management	**1- Assess the clinical picture and manage them** e.g., hypertension, arrhythmias, renal failure, and dehydration. **2- Decrease serum Ca^{++} level** to acceptable levels i.e., < 14 mg/dL = 7 mEq/L = 3.5 mmol/L by: • Hydration with normal saline (150 ml/h) + diuresis with furosemide (1-2 mg/kg i.v.) (avoid thiazide diuretics as they increase Ca^{++} level). • Other drugs and methods are rarely used: plicamycin (*mithramycin*), glucocorticoids, calcitonin, hemodialysis, and emergency parathyroidectomy in resistant cases. Di-sodium etidronate i.v. is the drug of choice in life-threatening hypercalcemia by inhibiting bone resorption. **3- Premedication:** Sedatives: are decreased due to central nervous changes.	**1- Assess the clinical picture and manage them** e.g., inspiratory stridor, hypotension, and congestive heart failure. **2- Increase serum Ca^{++} level by:** • I.v. Ca^{++} gluconate 10% 10 mL in acute cases. • Oral Ca^{++} and vitamin D in chronic cases. • Thiazide diuretics that increase Ca^{++} level. • Exogenous PTH replacement that is not yet practical for clinical use. **3- Premedication:** Sedatives: are decreased due to central nervous changes.
Intraoperative Management	• **Avoid ketamine** due to hypertension and personality changes. • Precautions of **renal failure and hypertension.** • **Avoid hypoventilation** because it causes acidosis, which increases the ionized Ca^{++}. • Use **muscle relaxants cautiously** due to their unpredictable response because increased Ca^{++} causes muscle weakness. • **Osteoporosis,** which may cause: ▫ **Vertebral compression** during laryngoscopy. ▫ **Bone fracture** during positioning or transport. ▫ Postoperative **hypocalcemic tetany**.	• **Avoid anesthetics,** which depress the heart. • Precautions of **congestive heart failure** are taken if it is present. • **Avoid hyperventilation** (or $NaHCO_3$ therapy) because it causes alkalosis, which decreases the ionized Ca^{++}. • Use **muscle relaxants cautiously** as there is increased sensitivity. • **Citrate containing blood products should be given slowly** in patients with preexisting hypocalcemia. • **Avoid 5% albumin solutions**, which may bind and decrease ionized Ca^{++}. • **Increased risk of coagulopathy** (as Ca^{++} is needed for coagulation cascade).
Postoperative Management	It is similar to those described above for subtotal thyroidectomy.	

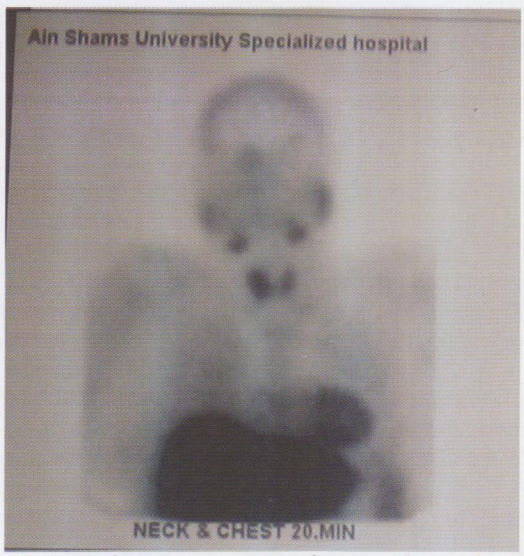


Figure 23-6: Radioisotope scan of a parathyroid adenoma

The Adrenal Gland

The adrenal gland is formed of adrenal cortex and adrenal medulla. The adrenal cortex is derived from mesodermal cells while adrenal medulla is derived from the chromaffin ectodermal cells of the neural crest.

A) Adrenal Cortex:

The adrenal cortex is formed of 3 zones, which secrete 30 different corticosteroids. The most important are:

- **Zona glomerulosa:** secretes **aldosterone** that is regulated by the renin-angiotensin system and serum potassium. Aldosterone **increases Na^+ and H_2O retention and increases H^+ and K^+ excretion**.
- **Zona fasciculata:** secretes **cortisol** that is under control of adreno-corticotropic hormone or corticotropin (ACTH). The ACTH is under control of corticotropin-releasing hormone (CRH). The action of cortisol is discussed in the chapter of "Pharmacological Adjuncts to Anesthesia and Intensive Care".
- **Zona reticularis:** secretes sex hormones.

	Mineralocorticoid Excess (Hyper-Aldosteronism)	Mineralocorticoid Deficiency (Hypo-Aldosteronism)
Causes	**1- Primary Hyperaldosteronism (Conn's syndrome)** e.g., adenoma, hyperplasia, carcinoma (with low renin level) **2- Secondary Hyperaldosteronism**: There is increased renin angiotensin with increased aldosterone secretion e.g., • Congestive heart failure. • Liver cirrhosis (and ascites). • Nephrotic syndrome. • Renal artery stenosis (reno-vascular hypertension).	**1- Atrophy or destruction** of both adrenal glands: It causes **combined** mineralocorticoid and glucocorticoid deficiency **(Addison's disease).** **2- Isolated** mineralocorticoid deficiency: due to • Unilateral adrenalectomy. • Diabetes mellitus • Heparin therapy. • Congenital deficiency. • Hypo-reninemia due to a defect in juxta-glomerular apparatus or treatment with angiotensin converting enzyme inhibitors. • Indomethacin-induced prostaglandin deficiency.
Clinical Picture	**1- Due to increased Na^+ retention; hypernatremia** may occur but Na^+ is usually slightly elevated. **2- Due to increased H_2O retention; hypervolemia (and hypertension)** and headache, which may cause congestive heart failure. **3- Due to increased K^+ excretion; hypokalemia** may occur, which causes muscle weakness and cramps. If it is prolonged, hypokalemic nephropathy (with polyuria) may occur. **4- Due to increased H^+ excretion; metabolic alkalosis** may occur, which decreases serum ionized Ca^{++} resulting in tetany.	**1- Due to increased Na^+ excretion; hyponatremia** may occur. **2- Due to H_2O excretion; hypovolemia (and hypotension)**, which may cause shock. **3- Due to increased K^+ retention; hyperkalemia** may occur, which causes heart block (any increase in serum K^+ without renal impairment is suggestive of hypo-aldosteronism). **4- Due to increased H^+ retention; metabolic acidosis** may occur, which increases serum ionized Ca^{++}.
Anesthetic management	**1- Anesthetic problems are detected from the clinical picture and causes:** for examples: • Manage hypertension, congestive heart failure, and volume status. • Correct fluid and electrolyte imbalance. K^+ syrup 2-6 g/day orally is used for hypokalemia. **2- Spironolactone:** • Aldosterone antagonist. • K^+ sparing diuretics. • Antihypertensive. 3- Surgical excision for aldosterone-secreting tumor (i.e. uni-or bilateral adrenalectomy) may be indicated according to sites of tumor. Bilateral excision requires exogenous administration of cortisol.	**1- Anesthetic problems are detected from the clinical picture and causes:** for example: • Manage hypotension and shock. • Correct fluid and electrolyte imbalance. **2- Exogenous mineralocorticoid** • Fludrocortisone (*Astonin-H or Cortilon*) 0.1-0.3 mg/day.

	Glucocorticoid Excess (Cushing's Syndrome) (Hyper-Adrenocorticism)	Glucocorticoid Deficiency (Hypo- Adrenocorticism)
Causes	**1- Exogenous** administration of steroid or ACTH. **2- Primary:** intrinsic hyperfunction of adrenal cortex e.g., adrenocortical adenoma or carcinoma. **3- Secondary: The term Cushing's disease** is reserved for Cushing's syndrome due to pituitary basophil micro-adenoma, which secretes ACTH. **4- Ectopic ACTH syndrome** as ACTH is secreted from non-pituitary tumors e.g., lung (especially small-cell carcinoma), kidney, and pancreas carcinoma.	**1- Primary** adrenal insufficiency **(Addison's disease)** due to destruction of adrenal gland (signs and symptoms occur when 90% of gland is destroyed) e.g., • Autoimmune disease (the most common cause). • Secondaries. • Tuberculosis. • Acute hemorrhage in the gland with meningo-coccal septicemia (Waterhouse-Friedricksen syndrome). Primary adrenal insufficiency causes combined mineralocorticoid and glucocorticoid deficiency. **2- Secondary** adrenal insufficiency due to decreased ACTH secretion from the pituitary gland e.g., • Exogenous glucocorticoid withdrawal (see later) • Hypopituitarism. Secondary adrenal insufficiency causes only glucocorticoid deficiency (without mineralocorticoid deficiency).
Clinical Picture (figure 23-7)	**1- Systemic hypertension.** **2- Hyperglycemia.** **3- Musculoskeletal system:** • **Osteoporosis**; therefore, care should be taken during positioning and transport. • **Muscle weakness**; therefore; care should be taken with muscle relaxants. • **Central obesity** (and in between scapulae i.e., buffalo hump) **weight gain**, and abdominal striae. **4- Hypervolemia and hypokalemic metabolic alkalosis** due to mineralocorticoid action of glucocorticoids. **5-** Increased **skin pigmentation** by ACTH. This differentiates between primary and secondary. **6- Plethoric rounded face (moon face).** **7- Poor wound healing and increased infections.** **8- Hirsutism and menstrual disturbances** because ACTH increases androgen also. **9- Depression and insomnia**.	a. Clinical pictures due to **cortisol deficiency**: weakness, fatigue, hypoglycemia, hypotension, weight loss, anorexia, nausea, vomiting, and cutaneous and mucosal hyper-pigmentation. b. Clinical pictures due to **aldosterone deficiency**: hyponatremia, hypovolemia, hyperkalemia, and metabolic acidosis (as above).
Investigations	1- **Dexamethasone suppression test:** Dexamethasone will decrease cortisol level in normal patients < 5 µg/dL, but not in hyper-adrenocorticism. 2- **Increased urinary cortisol excretion** > 150 µg/day. 3- **Loss of diurnal rhythm of serum cortisol** (normally 10-25 µg/mL in the morning 2-10 µg/mL in the evening). 4- Increased ACTH indicates pituitary or ectopic causes. 5- **CT scan and MRI** can identify the location of the tumor, but do not identify the function of the adrenal cortex.	1- **ACTH stimulation test:** An ACTH analogue (*Synacthen*) 250 µg i.v. is given. Plasma cortisol is measured before and after ACTH analogue by 30 and 60 minutes. All steroids, except dexamethasone must be discontinued 24 hours before testing. • A normal ACTH stimulation test yields a > 200 nmol/L (usually 420-700 nmol/L) rise in plasma cortisol in normal persons and indicates the ability of the patient to mount a stress response. • A positive test demonstrates a poor response to ACTH and indicates impairment of the adrenal cortex. • Absolute adrenal insufficiency has a low baseline cortisol level, but a positive ACTH stimulation test. • Relative adrenal insufficiency has a higher baseline cortisol level, but a positive ACTH stimulation test. 2- Decreased serum cortisol level < 20 µg/dL.
Treatment	1- **Hypophysectomy** (removal of the pituitary) or **adrenalectomy** according to the cause. 2- **Steroid cover** should be given during bilateral adrenalectomy. **Fludrocortisone** 0.1-0.3 mg/day after bilateral adrenalectomy is also given. 3- **Aldosterone antagonist.**	***Steroid cover:*** *Cortisol 100 mg i.v. followed by 10* mg/hour i.v. infusion. **Fludrocortisone** 0.1- 0.3 mg/day is also given.
Anesthetic Management	• **Anesthetic problems are detected from the clinical picture and causes.** • **Etomidate** may transiently decrease the synthesis and release of cortisol by the adrenal cortex.	



Figure 23-7: Two patients with Cushing's syndrome; the left one is due to a primary disease while the right one with pigmentations of the face due to secondary disease (pituitary adenoma)

Acute Adrenal Insufficiency or Failure (Addisonian Crisis) (Hypothalamic-Pituitary-Adrenal Suppression)

Causes:

It occurs in steroid dependent patients whose steroid doses are not increased during periods of stress (e.g., infection, trauma, or surgery).

Relative adrenal insufficiency or critical illness-related corticosteroid insufficiency is a condition in which there is adrenal insufficiency that does not meet the traditional criteria for adrenal dysfunction or hypofunction, but the magnitude of the expected response to clinical illness and other stresses is reduced.

Clinical Pictures:

It is a medical emergency.

It has the same, but **more severe picture of hypo-adrenocorticism** up to circulatory collapse. There may be **unexplained** vasopressor-dependent **refractory hypotension** and **unexplained refractory high fever** without apparent cause, that does not respond to antibiotics.

Investigations:

They are the same as Addison's disease (see above).

Treatment:

a- Supportive:

- Urgent **i.v fluids** usually 1-2 liters **(glucose and normal saline)** with **arterial blood pressure and central venous pressure** monitoring.
- **Vasopressors as dopamine**.
- Correct electrolyte and acid base disturbances such as serum potassium.
- **Antibiotics** to cover the possibility of infection (which may provoke the crisis).

b- Replacement:

- Hydrocortisone 100 mg/6 h i.v. bolus or 100 mg i.v. bolus followed by a continuous infusion at 10 mg/h. The continuous infusion is better because it maintains the plasma cortisol at stress levels greater than 830 nmol/L (30 µg/dL). When the patient's condition stabilizes, the steroid dose is reduced with eventual conversion to an oral preparation.

Any other steroid equivalent such as dexamethasone 4 mg/6 h (see chapter of "Pain Management" for the table of corticosteroid drugs).

- Fludrocortisone 0.1-0.3 mg/day in primary adrenal insufficiency.

Anesthetic Management:

- **Anesthetic problems are detected from the clinical picture and causes** such as management of the shock.
- **Steroid cover** with or without fludrocortisone (as above).
- **Etomidate** should be **avoided** because it transiently inhibits the synthesis of cortisol in normal patients.

Perioperative and Intensive Care Steroid Cover

• The **normal** endogenous cortisol production is **15-30 mg/24 h** (following a circadian rhythm). **During stress** induced by **major surgery**, cortisol production is in the range **75-150 mg/day** yielding a plasma cortisol level of 30 to 50 µg/dL. The increase is rapid and levels remain elevated **for a variable period of time** (up to 72 h following cardiac surgery). Patients in the intensive care units may demonstrate plasma cortisol levels greater than 60 µg/dL.

• Surgery is one of the most potent and best-studied activators of the hypothalamic-pituitary-adrenal axis. The degree of activation of the axis depends on the magnitude and duration of surgery and the type and depth of anesthesia.

• Deep general anesthesia or regional anesthesia postpones the usual intraoperative glucocorticoid surge until the postoperative period.

• If steroids are abruptly withdrawn in the perioperative period, the manifestations of adrenal insufficiency may appear within 24 to 36 hours. For patients with a history of long-term steroid use, it may take 6 to 12 months from the time of discontinuation of the steroids for the adrenal glands to recover full function.

Indications of perioperative or intensive care steroid cover:

1- Hypothalamic-Pituitary-Adrenal (HPA) Suppression:

Steroids produce HPA suppression that differs according to the dose of the steroids and whether the patient is still on steroids or has stopped them.

Low-dose steroid treatment < 10 mg prednisolone/day usually carries little danger of **hypothalamic-pituitary-adrenal suppression** (HPA suppression). Treatment with **> 10 mg prednisolone (or equivalent)** produces risks of HPA suppression. This may occur after treatment **via the oral, topical, parenteral, nebulized, or inhaled routes**. These patients must be assumed to be suffering from an inability to mount a normal endogenous steroid response to stress and must be supplemented accordingly. These patients show a positive ACTH stimulation test.

a- Patients currently taking Regular Steroids:

Dose of the Steroid	Affection on HPA	The Required Steroid Cover
< 10 mg prednisolone/day (or other equivalent)	Assume normal hypothalamic - pituitary axis (HPA) what-ever the type of surgery is	No additional steroid cover required.
> 10 mg prednisolone/day (or other equivalent)	HPA suppression occurs. Minor surgery e.g., hernia	• Routine preoperative steroid or hydrocortisone 25 mg i.v. at induction
	Intermediate surgery e.g., hysterectomy, cholecystectomy, or colon surgery	• Routine preoperative steroid plus hydrocortisone 25 mg i.v. at induction. • Postoperative hydrocortisone 25 mg 6 hourly for 24 h.
	Major surgery e.g., cardiac surgery, liver surgery, or Whipple surgery	• As intermediate surgery, but the postoperative steroid is continued for 48-72 h.
	Intensive care unit with sepsis or shock	• Routine preoperative steroid plus i.v. hydrocortisone 50-100 mg/6-8 h for 48 h to 1 week taper.
High dose immunosuppression	HPA suppression is severe	The usual immunosuppressive dose should be continued until being able to revert to normal oral intake e.g., 60 mg prednisolone /24 h = 240 mg hydrocortisone/24 h.

b- Patients formerly taking Regular Steroids:

- If **< 3 months have elapsed** since stopped steroids, treat the patient as if on **steroids**.
- If **> 3 months have elapsed** since stopped steroids, **no** perioperative **steroid** therapy is **necessary**.
- If the patient has received steroid in doses equivalent to **> 20 mg/day of prednisolone** for **more than 3 weeks within the past year** he/she is considered to have HPA suppression (in some authors).

2- Patients **undergoing pituitary or adrenal surgery.**

3- Patients with Cushing's syndrome.

4- In intensive care unit, critically-ill patients are at risk, especially who have infection, systemic inflammation from tuberculosis, meningococcemia, human immunodeficiency virus, sepsis, and/or diffuse intravascular coagulation. The incidence is 30-40%. These patients require steroid supplementation.

B) Adrenal Medulla:

Adrenal medulla is a specialized part of the sympathetic nervous system that is capable of synthesizing norepinephrine and epinephrine.

Catecholamine Excess (Pheochromocytoma or Pheo)

It is a catecholamine-secreting tumor arising from **chromaffin cells**. Pheochromocytoma is characterized by:
- **10% extra-adrenal** as para-vertebral sympathetic chain (it is sometimes called a paraganglioma) and any area from the base of the skull to the anus where chromaffin cells exist and 90% from the adrenal medulla.
- **10% malignant** and 90% benign.
- **10% bilateral and** 90% unilateral.
- **10% familial (inherited) pheochromocytoma** as autosomal dominant, alone or with multiple endocrine neoplasm (MEN) syndrome (see later).
- **10%** in children, which is usually multiple, extra-adrenal, and bilateral.

N.B.: The word pheochromocytoma is derived from the Greek words for dusky; phaios, and color; chroma. In 1912, Pick noted that these tumors were stained by a deep rust color when treated with chromium salts.

Pheo secretes 85% norepinephrine and 15% epinephrine in most cases. Normally, the adrenal gland secretes epinephrine 85% and norepinephrine 15% i.e., inverse of the previous ratio. It also secretes dopamine in rare percent of tumors.

Clinical Pictures: usually appear at the 3rd - 5th decade of life. There is a triad of headache, palpitation and diaphoresis (i.e., increased sweating).

1- In **noradrenaline predominant** secreting tumors (85% of tumors), there is **decreased circulatory blood volume** (due to hypertension) resulting in:
- **Systolic and diastolic hypertension** with **reflex bradycardia** (due to affection of α-receptors by norepinephrine).
- **Hemoconcentration** (Hct > 45%) and pallor.
- **Orthostatic hypotension.**

2- In **adrenaline predominant** secreting tumors, there are **paroxysmal attacks** (in 45% of cases), lasting minutes to hours, of:
- **Hypertension** (may be sustained in 50% of cases) (especially **systolic hypertension and diastolic hypotension**) resulting in **headache** and intra-cerebral hemorrhage. Arterial blood pressure may be normal in 5% of cases.
- **Tachycardia and tachy-arrhythmias** (due to affection of β-receptors by adrenaline) resulting in **palpitation**.

3- **In both types** of tumors (adrenaline and nor adrenaline-secreting tumors), there are:
- Increased basal metabolic rate causing **excessive sweating and weight loss.**
- **Cardiomyopathy, congestive heart failure, ischemia, and infarction.**
- **Hyperglycemia** due to predominant α activity (which decreases insulin release and increases glycolgenolysis and gluconeogenesis) over β activity (which increases insulin release).
- **Renal impairment may be present.**

N.B.: ▫ Unexpected intraoperative hypertension and tachycardia are occasionally the first indication of an undiagnosed pheochromocytoma.
▫ Presence of a normal blood pressure despite increased catecholamine levels in the plasma indicates a decreased number of α receptors (i.e., down-regulation) in response to high catecholamine levels.

Investigations:

	Normal value	Pheochromocytoma
a) Blood:		
• Plasma catecholamines	< 500 pg/mL	> 2000 pg/mL
• Plasma normetanephrine	< 112 pg/mL	> 400 pg/mL
• Plasma metanephrine	< 61 pg/mL	> 220 pg/mL
b) Urine: (24 hour collection)		
• Total catecholamines	< 125 µg	> 1200 µg
• Norepinephrine	< 100 µg	increased
• Epinephrine	< 1 µg	increased
• Metanephrine (highest sensitive 99%)	< 1.6 mg	> 2.5 mg
• Vanillylmandelic acid (nonspecific test)	< 8 mg	> 10 mg

c) Clonidine suppression test: As a confirmation test in equivocal results 0.3 mg clonidine is given orally	Clonidine suppresses norepinephrine secretion in an essential hypertensive patient because clonidine decreases neuronal release of norepinephrine, but does not affect chromaffin cell release.	Clonidine does not suppress norepinephrine secretion.
d) Glucagon provocative test Glucagon stimulates the release of catecholamines from the gland and is only performed in patients with diastolic blood pressure < 100 mm Hg	It increases plasma catecholamine < 2000 pg/mL.	It increases plasma catecholamine > 2000 pg/mL within 1-3 minutes

Equivocal results are results in between the normal and pheochromocytoma results. They are 10% of cases.

e) Localization of the Tumor:

- CT scan for tumors > 1 cm in size.
- MRI can detect smaller-sized tumors (figure 23-8).

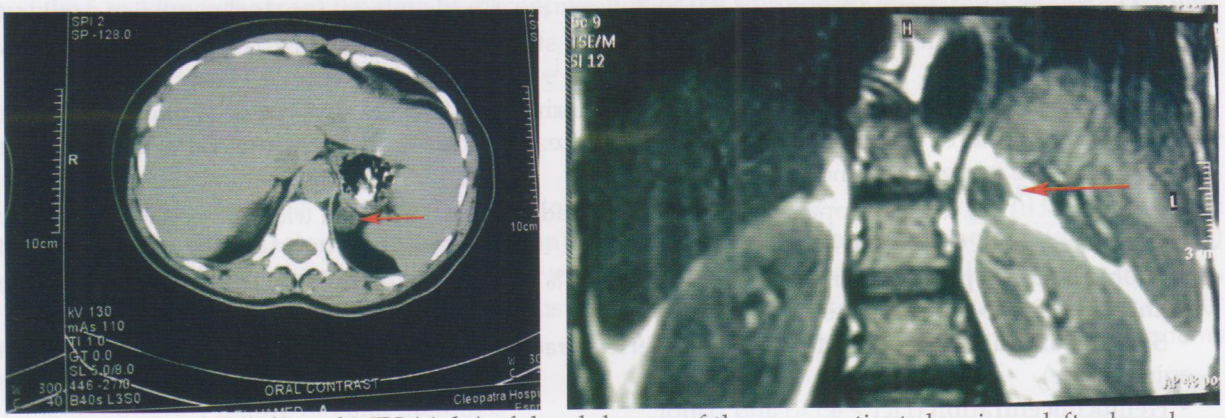


Figure 23-8: CT (left) and MRI (right) of the abdomen of the same patient showing a left adrenal adenoma

- Scintigraphy with ^{131}I-labeled metaiodobenzylguanidine (^{123}I-MIBG) is a very accurate functional test. ^{123}I-MIBG is an analogue of guanethidine, similar in structure to norepinephrine and taken up by adrenergic neurons and concentrated in catecholamine-secreting tumors. It is especially useful in detecting extra-adrenal pheo metastatic deposits, and confirming that an adrenal mass is a functional pheochromocytoma.
- Positron emission scan can also be used.
- Selective adrenal venous catheterization and sampling (for increased catecholamine concentration).

f) Investigations for Complications:

For example:
- serum glucose for hyperglycemia,
- echocardiography for heart function and
- renal function tests.

Differential Diagnosis:

- Thyrotoxicosis.
- Malignant hyperthermia.
- Diabetes mellitus.
- Malignant carcinoid tumor.

Theories of Hypertension and its control:

a- Conventional Theory:

- Although it is unsupported by scientific evidence, it states that hypertension occurs due to exposure of the arteriolar smooth muscle to norepinephrine (a neurotransmitter of the sympathetic system), which produces vasoconstriction.
- According to this theory, exogenous norepinephrine bathes the synapses directly. However if this was true, the sympathetic nervous system should be suppressed and the sympathetic nervous system activity should not be able to regulate blood pressure; instead, the circulatory hormones would do so.
- According to this theory (also unsupported), preoperative α-adrenergic blockade with phenoxybenzamine (see later) before tumor resection is used to control blood pressure. In addition, there are

mistaken beliefs that blood catecholamine concentrations correlate with blood pressure level and that hypertension occurs when the surgeon manipulates the tumor because this manipulation squeezes hormones out of the tumor and into the bloodstream.

Objections on this theory:

- Scientific data and clinical experience support contrary interpretations. Catecholamine concentrations do not correlate with the time of magnitude of blood pressure elevation, and preoperative treatment with nonselective α-adrenergic blockade for 2 weeks is commonly ineffective for the prevention of intraoperative hypertension.
- In theory, the nonspecific α-blocking agent, phenoxybenzamine, should not be the agent of choice because it has α_2-blocking properties. Because α_2 agonists generally produce bradycardia, sedation, and lower blood pressure, blocking the α_2 receptor will be expected to increase blood pressure and pulse. Nevertheless, phenoxybenzamine continues to be the agent most often recommended by many authors. Phenoxybenzamine is also very expensive, because it has no other clinical application.

b- An Alternative Recent Theory:

- The effect of chronic catecholamine excess is to amplify the sympathetic nervous system's response to all forms of noxious stimuli and trauma.
- Hypertension and tachycardia will be caused by the substantial stresses of laryngoscopy (not the induction of anesthesia as is often postulated) and the stress of surgical manipulations of any kind (not specifically tumor manipulation by the surgeon). These hemodynamic responses may be seen in any patient, but the effect seems to be exaggerated under the influence of chronic catecholamine excess. Such a theory is supported by animal data.

Therefore, the conventional regimen for controlling hypertension has changed to more recent recommendations (see later).

Anesthetic Management:

Preoperative Management:

Patient Preparation:

Aim: To control the systemic effects of the tumor then to remove it surgically.

A) Management of Hypertension:

According to the conventional theory of hypertension, patients with pheochromocytoma are controlled with α-blockers then by β-blockers for 1-2 weeks before surgery as follows:

a) α-Adrenergic Blocking Agents:

They are used to decrease the peripheral vascular resistance resulting in a decrease in the arterial blood pressure. They include:

1- **Phenoxybenzamine** (*Phental*)**:** (a non-competitive, non-selective α_1 and α_2 blocker) is given either:

- **Orally: 10 mg/12 h.** It is increased by 10 mg increments until the diastolic blood pressure is stabilized at 90-100 mm Hg. Most patients require 60-250 mg/day. Treatment should continue **for 1-2 week before surgery** to achieve mild orthostatic hypotension, but it should be **discontinued 24 to 48 hours before surgery** to avoid vascular unresponsiveness immediately following removal of the tumor because phenoxybenzamine has a prolonged action on α-receptors.

or • **I.v. infusion for 3 days** before the surgery with intravascular volume monitoring by central venous pressure and hematocrit (Hct) which drops about 5% and i.v. colloids.

Advantages of phenoxybenzamine over other competitive antagonists such as prazocin or labetalol:

- **It is more efficient** to control the blood pressure even intraoperatively during tumor manipulation due to irreversible alkylation of α receptors.
- It has a longer duration of action due to irreversible alkylation of α receptors.

Disadvantages: Because phenoxybenzamine is $\alpha_{1,2}$ blocker, it may enhance catecholamine secretion through α_2 blockade, which will result in tachycardia.

2- **Phentolamine:** *(Regitin)*

It is used often intraoperatively to control hypertensive episodes.

3- **Prazocin** (*Minipress*) (competitive, selective α_1 antagonist)

It can be used instead of phenoxybenzamine. It is a shorter acting agent. It causes less tachycardia and is easier to titrate to a desired end-point than phenoxybenzamine. Initial doses of 1.0 mg/8 h daily orally may be increased to 8-12 mg/day to obtain the desired effect. It may be less effective in preventing hypertensive episodes in the perioperative period.

Other α_1 blockers such as doxazosin and terazosin can be used.

b) β-Adrenergic Blocking Agent:

It is used to control heart arrhythmias. It should always be used **after α blockers and appropriate fluid replacement** because if β blockers are given at first, unopposed α-action may occur resulting in severe hypertension, which causes heart failure due to:

- Increased afterload on the heart.
- No β_1 inotropic action.

For example: • Propranolol 10-60 mg/8 h orally.

• Labetalol (its β-blocking action predominates over α-blocking, which is not desirable in norepinephrine-secreting tumors, but more preferable for epinephrine secreting tumors).

• Atenolol or metoprolol can be used.

Recently, according to the alternative theory of hypertension: Suggested rules for perioperative management before pheochromocytoma (or paraganglioma) removal are as follows:

1- **Control blood pressure before surgery by any effective** regimen with which you have experience for patients with pheochromocytoma. The aim is to keep blood pressure in the range of:

120-160 mm Hg systolic blood pressure and

65-85 mm Hg diastolic blood pressure and then operation can be performed.

2- **No specific agent** (volatile or intravenous anesthetic) has been shown to be superior in terms of outcomes.

3- Use what you know best for **intraoperative hemodynamic control**. The choice could be inhalation anesthetics, sodium nitroprusside, or nicardipine with esmolol to control intermittent tachycardia. Phentolamine is not necessary to be used if the anesthesiologist is not familiar with it.

4- The common recommendation that antihypertensive therapy should be given for 2 weeks before the operation has not been tested in properly conducted clinical trials. Some authors recommend that there is no place for phenoxybenzamine in modern medicine, although others still recommend it.

5- Pheochromocytoma should be suspected if severe hypertension occurs after induction of anesthesia in a previously undiagnosed patient; do not proceed with surgery unless it is urgent or emergent. If the surgery is urgent or emergent, perform intraoperative hemodynamic control as above. Consider using local and regional anesthesia to supplement the general anesthesia.

N.B.: Other drugs can be used in patient preparation:

These drugs are used with phenoxybenzamine to attain cardiovascular stability. They include:

- **$MgSO_4$ infusion**; it inhibits release of catecholamines from the adrenal medulla and peripheral nerve terminals, reduces sensitivity of α-receptors to catecholamines, and produces a direct vasodilator and anti-arrhythmic actions.
- **Angiotensin converting enzyme inhibitors.**
- α_2 agonists such as **dexmedetomidine**.
- **Ca^{++} channel blockers** (calcium is a trigger for catecholamine release from the tumor and excess calcium entry into myocardial cells contributes to the catecholamine-mediated cardiomyopathy), or
- **α-methyl para-tyrosine (metyrosine)**, which inhibits tyrosine hydroxylase decreasing catecholamine synthesis 50-80%. It is given orally. Gradually increase the dose 0.5 g/day up to 4 g/day. It may cause diarrhea, sedation, fatigue, anxiety, depression, extra-pyramidal reactions, crystalluria, and tremors. It is suitable **for malignant and inoperable tumors** in addition to α- and β- blockers.

B) Correction of Hypovolemia:

Correction of hypovolemia is important because α blockers dilate the vascular bed. 1-2 units of blood and fluids are usually needed to increase the intravascular volume.

C) Assess Criteria of Adequate Preparation:

- Arterial blood pressure should be < 165/90 mm Hg for 24 hours before surgery.
- Orthostatic hypotension should be present, but arterial blood pressure on standing should not be < 80/45 mm Hg.
- ECG: free from ST and T changes for a period of 2 weeks (i.e., no ischemia).
- Premature ventricular contractions (PVCs) should not be > 1 every 5 min.

Premedication:

1- **Sedatives**: to prevent anxiety induced release of catecholamines.

2- Anticholinergics: **avoid atropine**. Scopolamine is used instead.

3- **α- and β- blockers** are **continued** until the day of surgery.

4- **Cortisone cover** is used, if bilateral adrenalectomy is planned or if hypoadrenalism is a possibility.

Intraoperative management:

Aim: Avoid drugs and maneuvers that increase catecholamine release.

Drugs avoided are:

1) Drugs that stimulate the sympathetic nervous system:

• Ephedrine • Ketamine • Diethyl ether • Cyclopropane

2) Drugs that inhibit the parasympathetic nervous system i.e., vagolytic agents:

• Atropine • Pancuronium • Gallamine

3) Drugs that increase the arrhythmic effect of catecholamines:

• Halothane.

4) Drugs that release histamine: (Histamine increases CA release from the tumor)

• Atracurium • d-Tubocurarine • Morphine • Meperidine

5) Other drugs:

• Suxamethonium because abdominal muscle fasciculations increase the intra-abdominal pressure which increases catecholamine release from the tumor.

• Metoclopramide.

• Chlorpromazine.

• Calcium because it increases release of catecholamines from the tumor.

• Droperidol *(Innovar)* because severe hypertension may occur. Although droperidol causes hypotension in normal individuals due to its α-blocking action, but it causes hypertensive crisis in pheochromocytoma. The exact mechanism is not clear but may be due to:

▫ It directly stimulates chromaffin cells of the tumor to secrete catecholamines.

▫ It antagonizes presynaptic dopaminergic receptors that normally inhibit catecholamine release from sympathetic nerve endings.

▫ It inhibits catecholamine reuptake.

These actions cause release of excessive amounts of catecholamines.

Maneuvers avoided are:

Fear, stress, pain, shivering, hypoxia, and hypercarbia.

Monitoring:

Monitoring is needed especially on induction, skin incision, and tumor manipulation. Besides the standard monitors:

• ECG (CM_5 configuration).

• Invasive blood pressure: is done under good sedation and local anesthesia on insertion to avoid sympathetic stimulation by pain.

• Central venous pressure and pulmonary artery pressure monitoring are done under good sedation and local anesthesia on insertion to avoid sympathetic stimulation by the pain.

• Arterial blood gases, serum glucose, and electrolytes should also be monitored.

• Trans-esophageal echocardiography if available.

Choice of Anesthesia:

A) Regional Anesthesia: (for excision of pheochromocytoma).

Disadvantages:

1- Although it blocks the sympathetic nervous system, postsynaptic α receptors still respond to the direct effects of sudden increase in circulating concentration of catecholamines.

2- Block of sympathetic nervous system exaggerates intraoperative hypotension occurring after ligation of veins draining pheochromocytoma (see later).

3- Intra-abdominal manipulation, if the tumor is in the abdomen, can interfere with the patient's spontaneous ventilation.

4- It is only suitable for the supine position.

B) General Anesthesia: (of choice)

Induction:

• Avoid pressor response with intubation e.g., by deepening of anesthesia. More details of avoiding the pressor response of intubation are discussed in the chapter of "Airway Management".

• Thiopentone or etomidate is given slowly to avoid hypotension.

Maintenance:

O_2/N_2O + volatile agents + muscles relaxants and controlled ventilation are usually used.

• Volatile agents: Isoflurane, enflurane, sevoflurane, or desflurane are safe, but **halothane should be avoided** because it potentiates ventricular arrhythmias.
• Opioids: Fentanyl, sufentanil, or alfentanil can be used safely, but morphine and meperidine should be avoided.
• Muscle relaxants: Vecuronium, rocuronium, or pipecuronium are safe, but **pancuronium, atracurium, or d-tubocurarine should be avoided.**

Intraoperative Complications and Precautions:

1- Intraoperative Hypertension, Tachycardia, and Arrhythmias:

They occur **during tumor manipulation** resulting in the release of catecholamines. They are treated by:
• Na nitroprusside, nitroglycerin, phentolamine, hydralazine, $MgSO_4$, or labetalol for hypertension.
• Propranolol, esmolol, or amiodarone for tachyarrhythmias as supraventricular tachycardia.
• Lidocaine for ventricular arrhythmias.
• Increasing the depth of anesthesia.

Hypertension may also **persist after removal of the tumor** (and postoperatively) because:
• Residual pheochromocytoma may be still present.
• Plasma catecholamine level does not return to normal until 7-10 days after surgery due to slow release of stored catecholamines from peripheral nerves.

2- Intraoperative Hypotension:

Hypotension occurs **after ligation of the veins** draining the tumor **on tumor removal** especially if inadequate intravascular volume is present. This is due to:
• an immediate decrease in plasma catecholamines (i.e., half-lives of norepinephrine and epinephrine are approximately 1-2 minutes) **with persistent fatigue of the vasoconstrictor mechanism.**
• vasodilation from residual α-blockade with phenoxybenzamine (due to its long half-life),
• Intraoperative fluid and blood loss especially with excessive third space loss (due to abdominal surgery), and
• Increased depth of anesthesia.

Hypotension is treated by
• i.v. volume expansion to a pulmonary capillary wedge pressure (if available) of 16-18 mm Hg that should be attained before tumor vein ligation.
• Phenylephrine or norepinephrine infusion.
• Inotropes such as dopamine
• Decreasing the depth of anesthesia.

3- Intraoperative Hypoglycemia:

Hypoglycemia is common after removal of the tumor because:
• Suppression of Beta cells of the pancreas disappears after tumor removal, which increases the insulin levels.
• Gluconeogenesis and glycogenolysis are no longer present.

Therefore, glucose-containing solutions should be given.

4- Laparoscopic Adrenalectomy:

Laparoscopic adrenalectomy is used for tumors less than 4-5 cm in size with the following precautions:
• Pneumo-peritoneum increases catecholamine and vasopressin levels resulting in more hypertension.
• CO_2 insufflation produces hypercarbia, which increases the sympathetic tone.

Both Pneumo-peritoneum and hypercarbia increase cardiac output and arterial blood pressure, but due to the decreased postoperative pain and the quicker postoperative recovery, laparoscopic adrenalectomy is a good alternative to the traditional surgery.

5- Intraoperative ultrasonography can be used to localize small, functional tumors and to perform adrenal-sparing procedures or partial adrenalectomies. Adrenal-sparing procedures are particularly valuable on removing bilateral adrenal pheochromocytoma.

N.B.: Adrenalectomy is done for:
• Conn's disease.
• Cushing's syndrome.
• Pheochromocytoma.

Intraoperative Fluid Therapy:

Types:
• **Lactated ringer's solution or normal saline** is a recommended fluid for use **prior to tumor removal** and a **dextrose-containing solution** should be added **after tumor removal** because plasma catecholamines immediately decrease following resection, insulin levels increase and hypoglycemia may occur.

• **Intraoperative fluid salvage** resulting in **post-resection hypertension** secondary to catecholamine-laden blood has been reported.

Amounts: **Adequate fluid therapy** is essential and is the major factor responsible for the reduction (i.e., <2%) in operative mortality.

Postoperative Management:

Patients are managed in the **intensive care unit** for continuous invasive monitoring for 12-24 hours postoperatively.

Postoperative Complications:

1- Postoperative Hypertension or Hypotension:

Although **most patients** become **normotensive** following complete tumor resection, **25% of patients** remains **hypertensive** postoperatively and may remain with sustained hypertension indefinitely. Other patients may have **postoperative hypotension.** See above the **causes** of hypertension and hypotension.

2- Postoperative Hypoglycemia:

As above.

3- Postoperative Somnolence:

Patient may be very somnolent in the first 48 hours due to:

- sudden removal of activating catecholamines.
- hypoglycemia.

Carcinoid Tumor and Syndrome

Carcinoid tumors are **entero-chromaffin tumors**, which secrete about 20 different vasoactive substances such as serotonin, kallikrein, histamine, prostaglandins, and substance P.

Sites:

• Most tumors arise in **the gastrointestinal tract especially jujeno-ileum, or colon/rectum**, but tumors can occur in any other areas. It leads to secretion of vasoactive substances, which reach the portal circulations then the liver where they are metabolized in the liver; therefore, systemic effects (and clinical picture) do not appear i.e., no carcinoid syndrome except if vasoactive substances amount exceeds the liver ability to inactivate them.

• Other tumors arise in **pulmonary, ovarian or hepatic secondaries**. They bypass the portal circulation; so, systemic effects (and clinical picture) appear i.e., carcinoid syndrome occurs. 20% only of carcinoid tumors cause carcinoid syndrome and 4% are malignant resulting in hepatic secondaries, which also cause the carcinoid syndrome.

Clinical Picture of Carcinoid Syndrome:

The clinical picture differs according to the main vasoactive substance produced, but the two most common symptoms are **flushing and diarrhea**.

1- Serotonin (5-Hydroxy-Tryptamine) (5-HT) is secreted in all tumors especially mid-gut tumors. 5-HT causes:

- **Vasoconstriction** resulting in coronary artery spasm and hypertension.
- **Increased intestinal tone** resulting in
  - chronic intermittent abdominal **pain** and
  - profuse **diarrhea** with water and electrolyte imbalance. The diarrhea is usually relieved by serotonin receptor antagonists (especially 5-HT_3 antagonists).
- **Hyperglycemia** because serotonin stimulates glycogenolysis and gluconeogenesis.
- **Hypoproteinemia and pellagra** due to tryptophan deficiency used in serotonin synthesis.
- **Right-sided heart failure** due to vascular and myocardial plaque formation, which causes pulmonary stenosis and tricuspid regurgitation. Lung metabolism of serotonin prevents affection of the left side of the heart, but left side heart failure can occur by bronchial carcinoid tumor.

2- Kallikrein and tachykinins (substance P, neuropeptide K, and substance K): act on plasma kininogen producing bradykinin). They cause:

- **Vasodilatation** resulting in hypotension and sudden onset of flushing of the face, neck, trunk, and upper limbs (i.e., **carcinoid flush = Red Man Syndrome).** It is precipitated by alcohol, blue cheese, chocolate, red wine, exercise, stress, and drugs as catecholamines.
- **Bronchospasm.**

3- Histamine: can cause:

- Vasodilatation (as above) with pruritis, which can be prevented by H_1- and H_2- receptor antagonists.

- **Bronchospasm.**
- **Dysrhythmias** e.g., atrial premature beats, and supraventricular tachycardia.

4- Prostaglandins cause:

- Vasodilatation (as above).
- Increased intestinal tone causing diarrhea.

5- Other substances such as ACTH, growth hormone releasing factor, 5-hydroxy-L-tryptophan (5-HTP), gastrin, insulin, somatostatin, and glucagon.

Carcinoid Crisis:

It is excessive release of vasoactive peptides, which can occur spontaneously or it is precipitated by hypotension, histamine release, sympathetic stimulation, stress, chemotherapy, or surgical manipulation. It is characterized by diarrhea, abdominal pain, intense flushing, bronchospasm, and cardiovascular instability such as tachycardia, hypotension, or hypertension. Most of these clinical pictures appear during anesthesia. It may be fatal if not treated.

Investigations:

Increase of **5-hydroxylindoleacetic acid** (5-HIAA) **in urine** (a serotonin metabolite) **> 27 mg/day** is diagnostic.

Anesthetic Management:

Preoperative Management:

1- Patient Preparation:

1- **Somatostatin** (*Somatostatin*) ($t_{1/2}$ is 1-3 min) or **a somatostatin analogue** such as **octreotide or lanreotide**.

Octreotide (*Sandostatin*)**:**

- Action: Somatostatin (or its analogues) is growth hormone release inhibitory hormone, but it also inhibits the release of vasoactive peptides; therefore, it protects against carcinoid crisis.
- The $t_{1/2}$ = 45 min (longer than somatostatin)
- Dose: 150-250 µg subcutaneously/8 h, which should be given 24 h before anesthesia and then continued throughout the procedure.
- Side effects: - short-term: pain at the injection site, discomfort, nausea, and vomiting.
  - long-term: gallstones, steatorrhea, and deterioration in glucose tolerance.

2- **Anti-serotonin drugs ($5\text{-}HT_1$, $5\text{-}HT_2$, and $5\text{-}HT_3$):**

They can control diarrhea not flushing e.g.,

- Serotonin receptor antagonists such as methysergide, ketanserin, or cyproheptadine. Ondansetron (a $5\text{-}HT_3$ antagonist) is also useful as antiemetic.
- Inhibitors to serotonin synthesis as α methyldopa.

3- **Anti-kallikrein drugs** e.g., corticosteroids or aprotinin.

4- **Anti-histaminic drugs** can control flushing e.g., H_1 and H_2 blockers.

2- Symptomatic Treatment:

- Salbutamol and/or aminophylline to treat bronchospasm.
- Loperamide or diphenoxylate to treat diarrhea.
- Digitalis and diuretics to treat right-sided heart failure.

For actions, doses, and side effects of these drugs, see chapter "Pharmacological Adjunct to Anesthesia & Intensive Care".

3- Assess Cardiovascular Function for Heart Failure.

Patients may need preoperative valve replacement.

Intraoperative Management:

Monitoring:

Besides the standard monitors, the following monitors may be needed:

- Invasive arterial blood pressure.
- Central venous pressure and pulmonary capillary wedge pressure.

Choice of Anesthesia:

A) Regional Anesthesia:

Spinal or tense epidural anesthesia is **not preferred** as this may cause hypotension, which precipitates carcinoid crisis. **Epidural analgesia** with administration of **diluted local anesthetics** in a graded manner

or with **opioids** is a good choice provided that there is no hypotension, no perioperative stress and fear, and there is **good sedation**.

B) General Anesthesia:

Induction:

Etomidate, fentanyl (sufentanil, alfentanil, or remifentanil) and muscle relaxants e.g., vecuronium, cis-atracurium, or rocuronium are good choices because they are not known to release mediators.

Avoid i.v. agents such as propofol or thiopentone because they may cause hypotension and precipitate carcinoid crisis.

Maintenance:

O_2/N_2O + Fentanyl + Muscle relaxant with controlled ventilation are usually used.

- **Inhalational agents are avoided** as they may cause hypotension and may result in release of mediators. **Desflurane may be the best choice** in patients with liver metastasis because of its low rate of metabolism.
- Opioids such as **morphine are avoided** as they cause histamine release.
- Muscle relaxants as **atracurium or tubocurarine are avoided** as they cause histamine release.
- Mechanical ventilation is better by **a flow-generator type ventilator**, which can deliver inspired gas at high pressures if bronchospasm occurs.

Intraoperative Complications:

Carcinoid crisis with severe hypotension, hypertension, and/or bronchospasm may occur.

Avoid factors that precipitate carcinoid crisis such as:

- **Avoiding hypotension;** therefore, avoid tense regional anesthesia, i.v. and inhalational agents, deep anesthesia, and hypovolemia (increased by diarrhea). It is treated by volume expansion.
- **Avoiding histamine release;** therefore, avoid morphine, succinylcholine, mivacurium, atracurium, and tubocurarine.
- **Avoiding sympathetic stimulation,** (it increases catecholamines, which stimulate kallikrein); **therefore,** avoid ketamine, epinephrine, norepinephrine, dopamine, isoproterenol, or other vasopressors as they may precipitate mediator release.

  If cardiovascular collapse occurs, **methoxamine** is the **recommended** one.
- **Avoiding surgical manipulation;** therefore, octreotide 50 µg i.v. and 50 µg subcutaneously is given before tumor manipulation. Other anti-mediators can be used as above.

Postoperative Management:

Intensive care unit admission and postoperative controlled ventilation may be needed.

Apudomas

Apudomas are tumors in amino precursor uptake and decarboxylation cells (APUD cells), which originate from the neuro-ectoderm and are present in the anterior pituitary glands, thyroid, adrenal medulla, gastrointestinal tract, pancreatic islets, carotid bodies, and lungs. Apudomas are either:

- Ortho-endocrine: They produce amines and polypeptides associated normally with constituent cells.
- Para-endocrine: They produce substances produced usually by other organs.

Tumors of APUD cells include pheochromocytoma, carcinoid tumors, insulinoma, gastrinoma, and VIPoma.

Pheochromocytoma and **carcinoid tumors** are examples of ortho-endocrine APUD cells tumors and are discussed above. Both occur in chromaffin cells.

Gastrinoma:

There is increased gastrin production due to tumor in the D cells of the pancreatic islets resulting in Zollinger-Ellison syndrome, severe peptic ulceration, and diarrhea, gastrointestinal bleeding, and electrolyte disturbances. It is treated by proton pump inhibitors.

VIPoma:

It is a very rare tumor, which is often small cell bronchogenic carcinoma leading to secretion of vasoactive intestinal peptide (VIP). VIP leads to Verner-Morrison syndrome, which is characterized by watery diarrhea, hypokalemia, achlorhydria, and hypovolemia.

Pituitary Gland

Physiological Considerations:

Pituitary gland is located in the sella turcica at the base of the brain. It is formed from:

a- Anterior pituitary: It is under control of the hypothalamus by **vascular** connections as hypothalamic hormones travel by the hypophyseal portal veins to reach the anterior pituitary (i.e., **adeno-hypophysis**).

b- Posterior pituitary: It is composed of terminal endings of neurons. They originate in the hypothalamus (supraoptic and paraventricular nuclei at the median eminence) where hormones are synthesized in these nuclei and then transported along the hypothalamic neuronal axons (pituitary stalk) for storage in the posterior pituitary (i.e., **neuro-hypophysis**).

Hypothalamic Hormones	Anterior Pituitary Hormones	Action
1- Growth hormone-releasing hormone 2- Growth hormone release-inhibiting hormone (somatostatin)	Growth hormone	Increases secretion of insulin-like growth factors
3- Prolactin release inhibitory factor (dopamine)	Prolactin	Stimulates lactation
4- Gonadotropin-releasing hormone	Follicle stimulating hormone (FSH) and luteinizing hormone (LH)	Increase progesterone secretion and ovulation in females and increase testosterone secretion and spermatogenesis in males
5- Corticotropin releasing hormone	Corticotropin or adreno-corticotropic hormone (ACTH)	Increases cortisol and androgen secretion
6- Thyrotropin releasing hormone	Thyrotropin or thyroid stimulating hormone (TSH)	Increases thyroid hormone secretion (T_3 and T_4).

Hypothalamic Synthesis Site	Posterior Pituitary Hormone (Storage Site)	Action
1- Supraoptic nuclei	Antidiuretic hormone (vasopressin).	Stimulates free-water reabsorption in the kidney
2- Paraventricular nuclei	Oxytocin.	Stimulates milk ejection and uterus contraction

Pituitary adenomas usually arise from cells of the anterior pituitary gland. They occur either alone or with other tumors of parathyroids and pancreatic cells as part of multiple endocrine neoplasia type I. Tumors are either:

- **Functional** i.e., hormone secreting; they are **early diagnosed** (with their size < 1 cm in diameter); hence they are often called **microadenomas**.
- **Non-functional;** they are usually **late diagnosed** when they become large and produce **compression symptoms** such as headache or visual changes; hence, they are called **macroadenomas** (> 1 cm in diameter).

Clinical Picture of Pituitary Tumors:

1- Increased intracranial tension symptoms such as headache, vomiting, and papilloedema. Some pituitary tumors may also present as **pituitary apoplexy**, which is the abrupt onset of headache, visual changes, ophthalmoplegia, meningeal irritation, and altered mental status secondary to hemorrhage, necrosis, or infarction within the tumor.

2- Compression or invasion of the surrounding structures:

- **Optic chiasma** (roof of sella turcica), which causes **visual field defects** (bi-temporal hemianopia).
- **Hypothalamus** (above chiasma), which causes **temperature and circulatory changes**.
- **Roof of the nose** (floor of sella turcica), which causes **rhinorrhea**.

3- Endocrine manifestations:

a- Due to functioning tumors:

- Increased growth hormone, which causes **acromegaly** in adults or **gigantism** in pre-pubertal age (see later).
- Increased ACTH, which causes **Cushing's disease** (see above).

• Increased Prolactin secretion (i.e., prolactinomas), which is treated initially with bromocriptine (a long-acting dopamine agonist.).

b- Due to compression on the gland itself:

• Decreased secretions of all hormones, which causes **panhypopituitarism** (common). The decrease in hormone secretion usually occurs in the following sequence:

▫ **Gonadotropin deficiency** is the first to occur resulting in impotence in males and amenorrhea in females.

▫ **ACTH deficiency** is the second to occur within 2 weeks resulting in secondary adrenal insufficiency, which leads to:

- Severe pallor (in contrast to pigmentation of primary adrenal insufficiency where the primary decrease in the adrenal function is associated with increased ACTH secretion, which in turn increases pigmentation.
- Fluid and electrolyte imbalance (is not marked as in primary adrenal insufficiency due to intact aldosterone secretion).

▫ **TSH deficiency** is the third to occur within one month resulting in secondary hypothyroidism.

Therefore, steroids and thyroxine should be administered.

• Decreased secretions of a single hormone resulting in mono-tropic deficiency, which is very rare e.g., **diabetes insipidus** (see later).

Investigations:

Enlarged sella turcica can be detected by **CT scan** or **MRI** (figure 23-9, and 23-10).

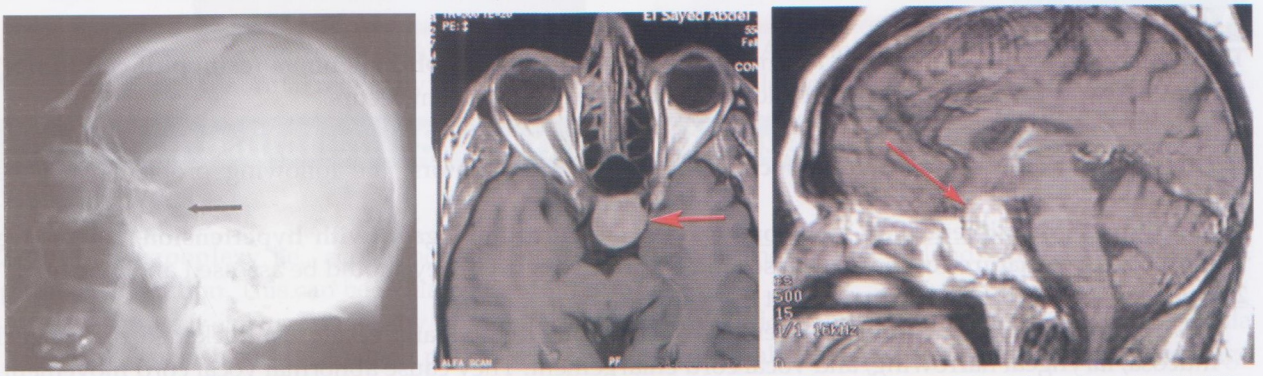


Figure 23-9: Plain x-ray skull (left), lateral view showing expanded sella turcica. Axial and sagittal MRI images of the sella turcica showing a pituitary adenoma

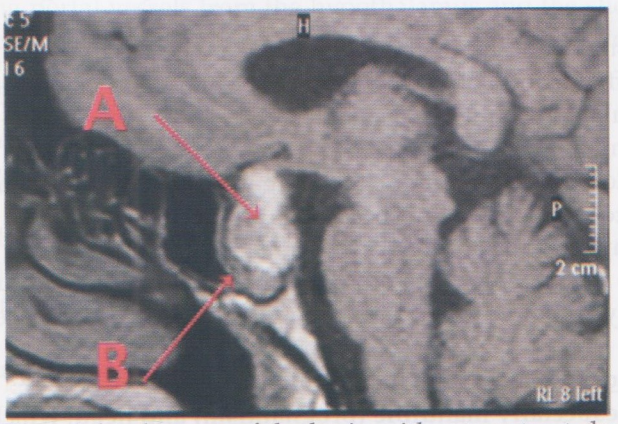


Figure 23-10: Sagittal MRI T1 weighted image of the brain without contrast showing a pituitary adenoma with pituitary apoplexy –pituitary hemorrhage- (A). The hemorrhage appears hyper-intense (white) and compresses the pituitary tissue which appears as a grey peripheral rim (B)

Surgical Approaches are either:

a- Bi-Frontal Craniotomy:

It is indicated for tumors **> 20 mm** in diameter with significant suprasellar extension.

Anesthetic management and problems are as these of craniotomy, that are discussed in chapter "Central Nervous Disease".

b- Transsphenoidal Approach:

It is indicated for tumors **< 10 mm** in diameter by using a microscope, via an incision in the gingival mucosa under the upper lip.

Anesthetic Problems:

1- Increased risk of infection due to working through the nose; therefore, prophylactic antibiotics are given.

2- Increased blood loss through the nose; therefore, mucosal injections of epinephrine-containing solution are needed.

3- Accumulation of blood and tissue debris in the pharynx and stomach; therefore, a pharyngeal pack and good suction are needed.

4- Injury to the surrounding structures:

a- Structures lateral to sella turcica:

- Injury to the **cavernous sinus**.
- Injury to the **internal carotid artery**.
- Injury to the **cranial nerves III, IV, V, and VI**.

b- Structures superior to sella turcica:

- Injury to the **optic nerve**; so, **visual evoked potential monitoring** may be needed.

5- Venous air embolism may occur because the patient position is usually supine with slightly head-up.

6- Associated pituitary dysfunction.

Acromegaly

There is an increase in the growth hormone secretion due to **acidophil adenoma** (**esinophil cell tumor**) after puberty. In pre-puberty, before fusion of the epiphysis, gigantism occurs.

Anesthetic Problems:

Besides the anesthetic problems associated with pituitary tumors, the following problems may be present:

1- Overgrowth of Viscera (i.e., Visceromegaly) such as **cardiomegaly, with hypertension, congestive heart failure, premature coronary disease, and cardiomyopathy**: They should be assessed and managed.

2- Overgrowth of Soft Tissue may result in:

- **Upper airway obstruction** due to enlarged mandible, tongue, and epiglottis, thickened pharyngeal mucosa, laryngeal narrowing, and vocal cord enlargement. They cause abnormal vocal cord movement, hoarseness of voice and even recurrent laryngeal nerve paralysis due to stretching by the overgrowth of the cartilaginous structures. This causes **difficult airway management, intubation and mask ventilation.** Therefore,
  - Preoperative assessment and indirect laryngoscopy are necessary.
  - Preparation for difficult intubation e.g., larger laryngoscope blades, smaller tube size, and even fiberoptic awake intubation should be available.
  - Elective tracheostomy may be needed.
  - Nasal intubation should be avoided due to enlargement of nasal turbinates.
  - Postoperative care to avoid airway obstruction is essential.
- **Peripheral neuropathy** e.g., carpal tunnel syndrome.
- **Compression of the ulnar artery;** therefore, **avoid intra-arterial cannulation in the radial artery** because there is usually impaired ulnar artery circulation (in 50% of cases), which may cause hand ischemia.

3- Overgrowth of Musculoskeletal System may result in:

- **Skeletal overgrowth especially mandible (prognathism) and head**, which causes difficult intubation and mask ventilation (figure 23-11).
- **Difficulties in regional anesthetic techniques**.
- **Osteoarthritis and osteoporosis;** so, care is taken during positioning.
- **Skeletal muscle weakness**; so, the non-depolarizing muscle relaxant doses should be decreased and a nerve stimulator should be used.

4- Increased intracranial tension resulting in headache, papilloedema, and visual disturbances.

5- Increased serum glucose level, which should be monitored and managed.

6- Hypothyroidism and hypoadrenalism may occur either post-hypophysectomy or secondary to the expanding tumor decreasing production of TSH and ACTH; therefore, **thyroxine hormone and steroids** may be given.

7- Some patients are on somatostatin analogues (octreotide or lanreotide) or bromocriptine, which are used to decrease growth hormone release. See above for their side effects.



Figure 23-11: An acromegalic patient (left). A comparison between a normal relatively large-sized hand and the enlarged hand of acromegaly

Panhypopituitarism (Simmond's Disease)

Causes:

1- Infection.

2- Pituitary apoplexy i.e., acute spontaneous hemorrhage in the pituitary gland, which usually causes pituitary infarction. This can be explained as follows:

- The pituitary is surrounded by bone inferiorly and on it sides in the hypophyseal recess (i.e., sella turcica) "Turkish saddle", which prevents its expansion and allows its compression when hemorrhage occurs.
- Much of the blood flow to the anterior pituitary consists of a low-pressure source of deoxygenated blood supplied by the long portal vessels from the hypothalamus and the short portal vessels from the posterior pituitary. These vessels are compressed when the pituitary is swollen where ischemia and infarction can occur.

Causes of pituitary apoplexy:

- Hemorrhage inside a large pituitary tumor.
- Postpartum hypotensive pituitary necrosis and infarction (i.e., Sheehan's syndrome); it occurs after postpartum hemorrhage.
- It is also associated with diabetes mellitus, hypertension, sickle cell anemia and acute shock.

4- Tumors of surrounding tissues e.g., **cranio-pharyngioma.**

5- Tumors of the gland itself e.g., **chromophobe adenoma.**

6- Skull fracture.

7- A sequel to a pituitary surgery (i.e., post-hypophysectomy).

Anesthetic Problems:

See above in pituitary adenoma with compression of the pituitary gland itself.

Diabetes Insipidus

There are two types of diabetes insipidus; neurogenic and nephrogenic. They share the same clinical picture and can be differentiated by the response to desmopressin.

Clinical Picture:

- Polyuria of poorly concentrated urine. Failure of urine osmolality to increase > 30 mOsm/L in the first few hours of complete fluid restriction is diagnostic of diabetes insipidus.
- Polydipsia.

• Increased plasma osmolality > urine osmolality.

	Central (Cranial) Diabetes Insipidus	Nephrogenic Diabetes Insipidus
Causes	Disease or damage affecting **the hypothalamic-posterior pituitary axis** resulting in a decrease in ADH secretion (the same causes of hypopituitarism as above)	ADH secretion is normal, but the **kidneys fail to respond to ADH,** which causes impaired kidney concentrating ability. It is due to: • **Congenital.** • **Acquired:** ▫ Chronic renal diseases. ▫ Sickle cell disease. ▫ Electrolyte disturbances e.g., hypokalemia, and hypercalcemia. ▫ Hyper-proteinemia. • **Drugs:** ▫ Methoxyflurane ▫ Mannitol ▫ Colchicines ▫ Lithium ▫ Amphotercin B ▫ Vincristine ▫ Demeclocycline
Investigations	Increase in urine osmolality after giving exogenous ADH, which is used as a confirmatory test.	No increase in urine osmolality after giving exogenous ADH, which is used as a confirmatory test.
Treatment	1- Treatment of the cause. 2- Fluid replacement either orally or intravenously. 3- ADH replacement: • **Aqueous vasopressin:** 5-10 units subcutaneously/4-8 h. It is of choice in **acute** cases. • **Vasopressin in oil:** 0.3 mL intramuscularly/day. It is long acting and may cause water intoxication. • **Desmopressin (DDAVP):** a synthetic analogue of ADH given intravenously or subcutaneously (2-4 µg/day) or intranasal spray 5-10 µg/6-12 h. It is long acting lasting 12- 24 h. It can be used in the outpatients and perioperatively. It lacks vasopressor effects.	1- Treatment of the cause 2- Fluid replacement either orally or intravenously. 3- Some authors try: • **Chlorpropamide (an oral hypoglycemic):** It potentiates ADH action. • **Thiazide diuretics:** They cause volume depletion, which produces paradoxic decrease in water delivery to renal tubules. This leads to decreased urine output. • Na^+ and protein restriction is needed to decrease urine output.

Q: What is the diuretic indication for patients with polyuria?

Inappropriate Secretion of Antidiuretic Hormone (ISADH)

Clinical Picture:

- The urine is concentrated and of low volume.
- The urine osmolarity is > plasma osmolality.

Causes: The ADH secretion is increased due to:

- Intracranial tumors.
- Hypothyroidism.
- Porphyria.
- Carcinoma of the lung especially undifferentiated small cell carcinoma.
- Postoperative increase in all patients.

Investigations:

1- Plasma: decreased osmolality, decreased serum Na^+ due to intravascular fluid expansion which causes dilution and cerebral edema.

2- Urine: increased osmolality and increased urine Na^+.

Treatment:

1- **Decrease fluid intake** to about 500 mL/day.

2- **Demeclocycline and NaCl infusion** are used to antagonize the ADH action.

3- **I.v. hypertonic saline** infusion is used to correct hyponatremia if it is severe where the serum sodium should be corrected in a rate of 0.5 mmol/L/h. Avoid rapid correction as it may produce central pontine myelinolysis.

4- **Vasopressin receptor antagonist such as conivaptan** acts by antagonizing the action of endogenous vasopressin at both V_{1A} and V_2 receptors. Conivaptan is given as an intravenous loading dose of 20 mg followed by a continuous infusion of 20 mg/day for 1-3 days.

Multiple Endocrine Neoplasia (MEN)

It is a group of syndromes characterized by tumor formations in several endocrine organs. It is usually hereditary.

Types:

1- MEN Type I: consists of 3 Ps;
- Pancreatic tumors (Gastrinoma or insulinoma).
- Pituitary tumors (chromophobes).
- Parathyroid tumors.

2- MEN Type II (Sipple's Syndrome): consists of:
- Medullary thyroid carcinoma; it secretes calcitonin, which decreases Ca^{++} and causes diarrhea.
- Pheochromocytoma.
- Parathyroid adenoma.

3- MEN Type III:
- Medullary thyroid carcinoma; it secretes calcitonin, which decreases Ca^{++} and causes diarrhea.
- Pheochromocytoma.
- Multiple mucosal neuroma with marfanoid appearance.

4- Other MEN:
- **Von Hippel-Landau syndrome** consists of hemangioblastoma of the retina, cerebellum, or other parts of the central nervous system, and pheochromocytoma.
- **Neurofibroma** may be associated with multiple neurofibromas, optic nerve glioma, Cafe'-lait spots, and axillary or inguinal freckling.
- **Pheochromocytoma-para-ganglionoma syndrome.**

N.B.: Pheochromocytoma is present either alone or as a part of MEN (see above). If multiple surgeries are planned for tumor excision, pheochromocytoma resection should be scheduled first.

Endocrine Emergencies (Crises)

They include:
- Diabetic ketoacidosis.
- Non-ketotic hyperosmolar hyperglycemic coma.
- Hypoglycemic coma.
- Thyrotoxic crisis (thyroid storm)
- Myxedema coma
- Tetany.
- Hypercalcemic crisis.
- Acute adrenal insufficiency (Addisonian Crisis)
- Pheochromocytoma.
- Carcinoid crisis.
- Pituitary apoplexy.

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Web Sites

- http://www.diabetes.org/

VASCULAR DISEASES

24

• Anesthesia for carotid endarterectomy • Minimally invasive carotid artery revascularization (endovascular surgical intervention of carotid disease) • Anesthesia for aortic surgery • Emergency aortic surgery	• Minimally invasive aortic surgeries a) Endo-luminal aortic stent-graft surgery (endovascular approach) b) Laparoscopic management of abdominal aortic surgery • Peripheral arterial surgeries and diseases • Peripheral venous surgeries and diseases • Amputations

Anesthesia for Carotid Endarterectomy

Carotid endarterectomy is the removal of atheromatous plaques from the vessel lumen. If the remaining intima is too thin, the vessel is closed with a vein or a synthetic Dacron patch. The most common site is at the carotid bifurcation or the proximal internal carotid artery.

Indications for surgical intervention include:

- Persistent unstable neurological status despite anticoagulation.
- Repeated TIAs or attacks lasting > 1 hour or minor stroke.
- Severe stenosis of the carotid artery (>70% occlusion) evident by angiography even without symptoms.

Pathology

Atherosclerotic Carotid Artery Disease

It is a part of atherosclerosis, which affects many arteries. It results in a decrease in cerebral blood flow up to complete obstruction of the carotid artery due to:

- **Embolism**: It occurs from any detached atherosclerotic plaque.
- **Hemorrhage:** It occurs due to rupture of the atherosclerotic carotid artery.
- **Thromboembolism**: It occurs when thrombosis occurs on the plaque, which narrows the lumen to a great degree.

On occlusion of one internal carotid artery e.g., due to embolism or clamping, the cerebral blood flow continues through **collaterals** such as:

1- The **opposite carotid system** via the anterior communicating artery.

2- The **vertebro-basilar system** via the posterior communicating artery.

3- Anastomosis **between the internal and external carotid vessels** around the orbit.

Therefore, the presence of developmental abnormalities or acquired occlusive disease in these vessels would predispose to cerebral infarction.

Clinical Picture

1- Cerebral Stroke

- It is a **neurological deficit** that lasts **more than 24 hours**. It usually causes hemiplegia due to focal cerebral infarction.
- It is caused by ▫ ischemic cerebrovascular strokes (thrombosis or embolism) (80%) and
  ▫ hemorrhage (20%).
- The clinical picture of the stroke depends on adequacy of the collateral circulation as emboli distal to areas of collateral circulation produce symptoms.

For example,

- ▫ Transient ischemic attacks usually precede the majority of thrombotic strokes.
- ▫ Transient monocular blindness due to small emboli in ophthalmic artery branches (Amaurosis Fugax).
- ▫ Contra-lateral motor and sensory deficits that primarily affect the arm and the face due to larger emboli, which usually enter the middle cerebral artery. Aphasia occurs if the dominant hemisphere is affected.

- Contra-lateral motor and sensory deficits that primarily affect the legs due to emboli in the anterior cerebral artery branches.

2- Transient Ischemic Attacks (TIAs)

- They are **neurological deficits that resolve within 24 hours**. They usually cause hemiparesis due to focal cerebral ischemia.
- They are caused by low flow states at a tightly stenotic lesion e.g., thrombosis or emboli that arise from the extracranial vessels or the heart.

3- Chronic Cerebral Ischemia.

4- Asymptomatic Carotid Bruit.

Anesthetic Management

Preoperative Management

Preoperative assessments are performed by history, examination, and investigations.

1- Preoperative Assessment for Detection of the Clinical Picture of Carotid Artery Disease:

- Assess the **perioperative mortality rate** which varies with the symptoms as the incidence of mortality is arranged in a descending manner as follows; frank stroke (6%), TIAs, chronic cerebral ischemia, and asymptomatic (0%).
- Assess the patient's **airway and ventilation** where the range of **the patient's tolerated neck motion** without evidence of cerebral ischemia should be determined, so that extreme extension and lateral rotation of the neck during ventilation can be avoided because these movements may occlude vertebral arteries and contribute to the postoperative neurological deficits.
- Detect preoperative risk factors, which increase the incidence of the postoperative stroke:
  - Active neurological process before the surgery.
  - Left-sided procedures.
  - Ipsilateral ischemic lesions on CT scan.
  - Contralateral carotid occlusion.
  - Impaired consciousness.
  - Poor collaterals.
  - An irregular or ulcerated ipsilateral plaque.
  - Endarterectomy done in conjunction with coronary artery bypass graft surgery.

2- Preoperative Assessment of Other Manifestations of Generalized Atherosclerosis:

Such as hypertension, ischemic heart, renal diseases…etc.

3- Preoperative Assessment of Other Coexisting Diseases:

The patient is usually **elderly and heavy smoker**; therefore, the patient may have:

- Pulmonary diseases e.g., chronic obstructive airway disease.
- Diabetes mellitus.
- Hypertension, ischemic heart and congestive heart disease.

It is still a controversy if the patient has both carotid and coronary diseases as the risk is increased in one of them if the other is done first. Some authors advocate the management of coronary disease first, but **most other authors** advocate the **management of carotid disease first by carotid endarterectomy or angioplasty to protect the brain before the patient is exposed to cardiopulmonary bypass.**

- Renal diseases.

These diseases must be properly assessed and managed preoperatively for maximal improvement because they increase perioperative morbidity and mortality.

4- Preoperative Drug Therapy:

All antihypertensive and antianginal treatment should be **continued until the day of surgery** (except diuretics) to avoid rebound phenomenon.

Aspirin may increase the bleeding time, but some authors advocate its usage before carotid endarterectomy.

5- Preoperative Investigations:

In addition to the standard investigations, the following investigations are useful:

- **Cerebral angiography** (figure 24-1).
- **Coagulation profile.**

• **Trans-cranial Doppler** to assess the changes in the middle cerebral artery blood flow velocity as a marker of cerebrovascular reactivity to CO_2.



Figure 24-1: Left carotid angiography showing severe concentric stenosis of the left internal carotid artery

• For associated diseases e.g., pulmonary function tests, arterial blood gas analysis, serum glucose, echo-cardiography, kidney function tests…etc.

Premedications:

1- Sedatives are given to avoid the increase in heart rate and blood pressure because both aggravate myocardial ischemia and neurological deficits. Sedation is performed by reassurance, diazepam 5 mg orally 1 hour preoperatively, or midazolam 3 mg intravenously.

Avoid over-sedation as it causes:

• respiratory depression; it increases $PaCO_2$ resulting in cerebral steal phenomenon, which in turn causes cerebral ischemia.

• hypotension.

• delayed awakening from anesthesia; therefore, it interferes with postoperative neurological assessment.

2- Anticholinergics e.g., atropine are avoided especially in ischemic heart disease due to the tachycardia produced.

Intraoperative Management

There is clamping of common, internal, and external carotid arteries during removal of atheromatous plaques and during arterial reconstruction; therefore, the major anesthetic problems include:

• Cerebral ischemia; so, avoid cerebral hypoperfusion.

• Myocardial ischemia; so, make balance between O_2 supply and demand.

Monitoring:

Besides the standard monitors, the following monitors are useful:

• ECG: CM_5 lead I configuration or automatic ST segment analysis are used to detect ischemia.

• Urine output.

• Temperature: by an esophageal or tympanic membrane probe.

• Cardiovascular monitors such as pulmonary artery pressure, central venous pressure, cardiac output measurement, and trans-esophageal echocardiography.

• Invasive arterial blood pressure.

• Arterial blood gas analysis.

• **Monitoring of Cerebral Perfusion** (is done at an early stage before clamping).

a) If Local (regional) anesthesia is used:

Repeated neurological assessment in **awake patients** after initial clamping of the aorta for the level of consciousness, speech, and contralateral motor power such as handgrip is the **most reliable and sensitive method.** It is the **gold standard** neurological monitoring.

Profound unconsciousness and subtle but immediate deficits **within 30 seconds** such as confusion, slurred speech, a delay in answering questions may occur on cross-clamping if the collateral perfusion is inadequate. Deficits after a variable period of time may be related to relative hypotension.

b) If general anesthesia is used:

None of the following methods is as reliable as repeated neurological assessment in awake patients. These methods include:

1- Jugular-Venous O_2 Saturation ($SjvO_2$):

$$\text{Cerebral blood flow (CBF)} = \frac{\text{Cerebral metabolic rate for } O_2}{SaO_2 \quad SjvO_2}$$

$$SaO_2 - SjvO_2 = \frac{\text{Cerebral metabolic rate for } O_2}{\text{Cerebral blood flow}}$$

$$SjvO_2 = SaO_2 - \frac{\text{Cerebral metabolic rate for } O_2}{\text{Cerebral blood flow}}$$

Where SaO_2 = arterial O_2 saturation.

$SjvO_2$ = jugular venous O_2 saturation.

As long as arterial O_2 content is constant, a decrease in the jugular venous O_2 saturation indicates either decreased CBF or increased cerebral metabolic rate of O_2 without a simultaneous increase in CBF.

It is **unreliable** because it is an accurate monitor of global rather than regional CBF.

2- Internal Carotid Distal Stump Pressure (Occlusion Pressure):

It measures the pressure in the portion of the internal carotid artery cephalad to the carotid cross-clamp. It **reflects the pressure transmitted through collateral vessels (in circle of Willis)** and thus the perfusion pressure in the ipsilateral internal carotid artery. It should be **> 25-50 mm Hg** to indicate adequate collateral circulation to avoid neurological injury (figure 24-2). Some physicians depend on observation of retrograde flow from the opened carotid artery.

Occlusion pressure is an **unreliable** monitor because:

- It does not correlate consistently with changes in electroencephalography (EEG), regional cerebral blood flow (rCBF), or changes in the neurological status of awake patients.
- Anesthetic agents can change the carotid stump pressure without changing rCBF. Therefore, it is not sufficiently sensitive or specific for shunting. If a shunt is done only based on stump pressure, some patients may have unnecessary shunts done.

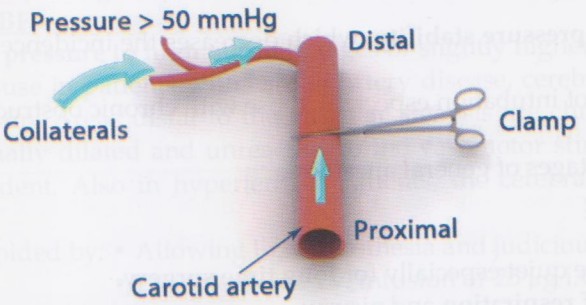


Figure 24-2: Stump pressure

3- Measurement of CBF:

CBF is measured either globally or locally. Most methods of measurement of CBF are restricted for research work only. **Trans-cranial Doppler** is the only method which can be used clinically.

Normally global CBF = 50 mL/100 g/min.

If global CBF is > 24 mL/100 g/min, it is considered adequate.

If global CBF is < 18 mL/100 g/min, it is considered inadequate.

Methods of measuring CBF are discussed in details in the chapter of "Monitoring for Anesthesia & Intensive Care".

4- Electroencephalography (EEG) Unprocessed or Processed:

Both unprocessed and processed EEG give an indication that there may be areas of the brain at risk of infarction i.e., cerebral ischemia. They can assess:

- The indication and the importance of the shunt before its construction and the function and patency of the shunt after placement.
- Cerebral tolerance to ischemia i.e., the adequacy of collaterals.
- Unexpected ischemia in other cerebral areas e.g., due to vertebro-basilar insufficiency from positioning or inadequate collaterals.

EEG is **unreliable** because it is **not sensitive or specific** in detection of cerebral ischemia. EEG changes that occur with hypothermia, hypoxemia, hypocarbia, and deep anesthesia mimic EEG signs of cerebral ischemia; therefore, if it is used alone it cannot predict the need for shunting or occurrence of post-operative neurological deficits.

5- Somato-Sensory Evoked Potentials (SSEPs):

They give an indication of areas of the brain at risk of infarction (cerebral ischemia). They can be used to detect cerebral ischemia when EEG recording cannot detect cerebral ischemia e.g., during barbiturate anesthesia because EEG becomes isoelectric indicating that the neurons are not functioning and therefore, are maximally protected, but it cannot detect whether these neurons are ischemic or not. SSEPs remain intact and therefore, would potentially be more useful as a clinical monitor.

They are **unreliable** because they are still not sensitive or specific to predict the need for shunting or occurrence of postoperative neurological deficits.

6- Trans-Conjunctival O_2 Tension:

It is **unreliable** because there is no correlation between trans-conjunctival O_2 tension and rCBF.

7- Cerebral Oximetry (Near-Infrared Spectroscopy):

It is used to assess changes in cerebral blood flow by measuring regional cerebral oxygenation (arterial, capillary, and mainly venous hemoglobin"Hb") as carotid artery clamping causes a variable decrease in cerebral HbO_2 saturation.

Choice of Anesthesia:

A) Regional Anesthesia:

One of the following methods or even a combination of them can be used.

- **Cervical plexus block (deep and superficial),**
- **cervical epidural anesthesia, or**
- **local infiltration.**

It is essential to provide sensory blockade of $C_2 - C_4$ dermatomes.

Sedation is usually needed by benzodiazepines (as midazolam) and opioids (as remifentanil).

Advantages of Regional Anesthesia:

- It allows repeated neurological assessment in **awake patients,** which is the **most reliable cerebral monitor**.
- It allows greater **blood pressure stability**, which decreases the incidence of perioperative myocardial infarction.
- It avoids complications of intubation especially those with chronic obstructive airway disease.

Disadvantages:

It is the opposite of advantages of general anesthesia.

B) General Anesthesia:

Advantages:

- It allows the patient to be quiet especially for **long time surgery.**
- It allows early **control of respiration** and airway.
- It allows **brain protective measures** to be taken.
- **It avoids excessive neck palpation** (which could occur during performing local anesthesia) because regional anesthesia can lead to dislodgement and subsequent embolization of a portion of plaque.

Disadvantages:

It is the opposite of advantages of regional anesthesia.

Induction:

Smooth induction is usually indicated with the following considerations:

- Preoxygenation with 100% O_2 for 5 min is essential.
- Thiopentone or etomidate can be used.
- Nondepolarizing **muscle relaxants without cardiovascular effects,** as vecuronium or cis-atracurium, are preferred.
- **Avoid suxamethonium in hemiparetic patients** for the possibility of hyperkalemia.

• **Avoid the pressor response to intubation**. It is discussed in the chapter of "Airway Management".

Maintenance:

O_2/N_2O (5:5), a volatile agent, an opioid, a muscle relaxant, and controlled ventilation are usually used.

• Light anesthesia is preferred than deep anesthesia because:
  ▫ It allows ischemic patterns on EEG to be recognized easily.
  ▫ It allows better SSEPs interpretations.
  ▫ It allows good maintenance of the patient's arterial blood pressure.
  ▫ It is associated with a decreased incidence of perioperative cardiac infarction.

• O_2/N_2O (50%) is usually used. Avoid 100% O_2 as it causes cerebral vasoconstriction. N_2O is stopped before opening the vessels to avoid air embolism.

• Volatile agents: **Isoflurane, sevoflurane, and desflurane are of choice.** Both isoflurane and halothane are cerebral vasodilators and increase CBF, but critical CBF (rCBF at which, EEG pattern of ischemia becomes apparent) is as follows: With isoflurane, it is < 10 mL/100 g brain tissues/min.
With halothane, it is 18-20 mL/100 g brain tissues/min.

Therefore, isoflurane has some cerebral protective effect against focal ischemia and may be the best volatile anesthetic agent used in carotid endarterectomy. High doses of isoflurane (if used alone) cause hypotension and tachycardia, which can precipitate myocardial ischemia in those patients; so, low doses of isoflurane are used with opioids to provide hemodynamic stability.

• Controlled ventilation:
  ▫ **Before repair of carotid stenosis**, it is recommended to maintain **normocarbia or mild hypocarbia** because hyperventilation causes hypocarbia resulting in respiratory alkalosis. Hypocarbia causes inverse cerebral steal (Robin Hood phenomenon) by inducing vasoconstriction of the normal reactive vascular beds in the normally perfused regions of the brain. This causes diversion of the blood to the maximally dilated unreactive vascular beds in the hypoperfused regions of the brain; so, hypocarbia has been recommended during carotid endarterectomy, but it causes respiratory alkalosis which shifts the O_2-Hb dissociation curve to the left. This decreases O_2 delivery to the brain cells and exacerbates cerebral ischemia. Nowadays, it is believed that extreme hypocarbia is detrimental to the brain cells. Also increased $PaCO_2$ produces cerebral steal phenomenon.
  ▫ **After repair of carotid stenosis**, some authors recommend **hypocarbia** (and hypotension) to decrease CBF, because some patients may develop **marked hyperemia** with CBF of 100 mL/min/100 g brain tissue. If CBF is not decreased, these patients are at a risk of postoperative intra-cerebral hemorrhage.

Intraoperative Problems and Considerations:

1) Brain Protection Measures: (during the period of carotid clamping)

A- Measures to increase CBF:

1- **Elevate arterial blood pressure to high normal range**s or slightly higher 15-25% above upper limits (up to 170 mm Hg) because in patients with carotid artery disease, cerebral autoregulation is lost in ischemic areas of the brain. Areas distal to the vascular stenosis are chronically hypoperfused and blood vessels are maximally dilated and unreactive to the vasomotor stimuli; so, perfusion in these areas is pressure dependent. Also in hypertensive patients, the cerebral autoregulation is reset at higher limits.

- Hypotension can be avoided by: • Allowing light anesthesia and judicious amounts of i.v. fluids.
  • Phenylephrine i.v. infusion or 25 µg i.v. increments.
- Extreme increases in arterial blood pressure are avoided by:
  • Nitroglycerin infusion; it is of choice because it produces coronary vasodilation too, or
  • Na nitroprusside infusion.

Because elevated blood pressure may precipitate myocardial ischemia and left ventricular failure in patients with carotid artery diseases as 30-50% of these patients have with coronary artery diseases, some authors do not recommend maintaining a slight increase in arterial blood pressure in patients with coronary artery disease, except if there is evidence of cerebral ischemia.

2- **Ca^{++} channel blockers such as nimodipine;** it has a vasodilator effect especially on cerebral vessels; so, it protects against focal ischemia.

3- **Decrease intracerebral pressure ICP by dehydrating measures.**

4- Hemodilution is advised to maintain hematocrit at 30%.

B- Measures to decrease Cerebral Metabolic Rate of O_2 ($CMRO_2$):

1- Anesthesia by **isoflurane or sevoflurane as both decrease the critical CBF** (i.e., CBF at which ischemia occurs) as compared to halothane and enflurane.

2- **Hypothermia** up to core temperature of 30°C (not used nowadays), but hyperthermia should be avoided.

3- **Anticonvulsants.**

4- **Barbiturates as thiopentone;** 5mg/kg/h or 50 mg increments (total dose 500-1500 mg) to avoid hypotension. EEG monitor should be used to achieve and maintain burst suppression pattern. When EEG becomes isoelectric, it indicates non-functioning neurons. Further doses of thiopentone will not provide additional cerebral protective effects. Thiopentone is beneficial in protection of **focal (but not global)** ischemia. Some authors do not recommend it in carotid endarterectomy because:

- **EEG becomes a useless monitor** for cerebral ischemia due to the isoelectricity induced by thiopentone.
- Doses of thiopentone required to suppress EEG **may cause hypotension and delayed awakening.**

C- Others Measures:

1- **Control $PaCO_2$** as above.

2- **Bypass (temporary) shunt:** can be constructed between the common carotid artery and distal internal carotid artery. Disadvantages of the shunt:

- It does **not guarantee** an adequate CBF.
- It makes the surgical technique **more difficult**.
- It may cause **plaque embolization, thrombo-embolism, air embolism**, or intimal dissection.

3- **Hyperbaric O_2;** it increases cerebral O_2 delivery and causes vasoconstriction in normal brain tissues.

4- **Heparinization:** 5000-10 000 IU heparin i.v. before carotid occlusion then reversal by protamine 50-75 mg before skin closure.

5- **S (+) ketamine** is neuro-protective because it is a more potent N-methyl D-aspartate (NMDA) receptor antagonist than the racemic mixture of ketamine, which is commercially available.

6- **Dexmedetomidine** is neuro-protective although it decreases CBF.

2) Intraoperative Hypo – or Hypertension:

It can occur intraoperatively and needs adjustment the depth of anesthesia or administration of a vasodilator or a vasopressor after searching for the possible cause.

3) Intraoperative Arrhythmias:

a) Reflex Bradycardia:

It occurs due to **manipulation of the carotid sinus by the surgeon**.

Treatment:

- Prophylactic infiltration of the carotid sinus by lignocaine, but this itself may cause bradycardia.
- I.v. atropine.

b) Reflex Tachycardia:

Treatment: β-blockers.

4) Reperfusion Injury (Hyper-reperfusion Syndrome):

Patients having the greatest degrees of carotid stenosis and the greatest degrees of pressure drop across the stenosis are at the highest risk of reperfusion injury affecting ischemic brain tissues > normal brain tissues. This syndrome occurs because areas of the brain distal to the carotid stenosis are:

- Chronically hypoperfused and their vascular beds are maximally dilated.
- Unresponsive to vasomotor stimuli.
- Lacking autoregulation response to pressure changes; so, the blood flow in these areas is pressure dependent.

Therefore, after repair of carotid stenosis, blood flow to these areas is resumed and perfusion pressure is markedly increased. Because the auto-regulatory mechanisms are lost, CBF is increased in response to the increase in perfusion pressure.

Clinical pictures include headache, signs of transient cerebral ischemia, seizures, brain edema, and even intra-cerebral hemorrhage occurs after the repair.

Treatment is mainly prophylactic. Maintain arterial blood pressure at low normal ranges after the repair of carotid stenosis and the release of carotid cross-clamp (this also decreases the stress on the carotid suture line).

5) Intraoperative Fluid Therapy:

Amount: It is better to be limited to 10-15 mL/kg/h in addition to compensation of any blood losses.

Avoid over-hydration because it may lead to postoperative hypertension and congestive heart failure in patients with coexisting heart disease.

Types: • Normal saline.
• Colloid or blood for blood loss.
• **Avoid dextrose-containing solutions** because hyperglycemia worsens the neurological outcome after cerebral ischemia.

Recovery and Extubation:

Smooth rapid recovery is needed to allow **immediate neurological assessment,** but it may cause hypertension or tachycardia, which requires treatment.

Postoperative Management and Intensive Care Considerations

Fast-Track Recovery

Routinely, patients are admitted to ICU for 24 hours to monitor postoperative complications and they stay in the hospital for a few days.

Recently, most patients undergo fast-track recovery as there is no need for ICU and they are allowed early home discharge after 1-2 days. This can be achieved by the use of short acting agents such as propofol, sevoflurane, and atracurium.

Postoperative Complications:

1) Delayed Recovery from General Anesthesia (or Postoperative Neurological Dysfunction):

1- **Exclude causes** as hypoglycemia, hyperglycemia, hypothermia, hypoxia, hypercapnia, and anesthetic over-dosage.

2- The **patency of the carotid artery on which the surgery was performed should be evaluated** in the operating room by **Doppler studies**.
• If there is no blood flow in the carotid artery, the incision should be immediately re-explored.
• If there is normal blood flow in the carotid artery, intraoperative cerebral infarction should be considered.

The patient should remain intubated until other diagnostic procedures as CT scan and cerebral angiography are done.

3- Search for other causes as **adverse intraoperative events** e.g.,
• Intraoperative embolism (the most common cause).
• Intraoperative thrombosis.
• Recurrent stenosis.
• Intra-cerebral hemorrhage.
• **Postoperative hyper-perfusion syndrome**; therefore, proper control of postoperative hypertension is essential.
• Intraoperative hemodynamics that may decrease CBF as shunts problems, carotid clamping, intra-cerebral occlusive disease.

2) Appearance of New or Increased Preexisting Neurological Deficits:

For example: • Cranial nerve dysfunction VII, IX, X, XII (IX, X need intubation).
• Recurrent laryngeal nerve injury resulting in hoarseness of voice, impaired cough, and respiratory insufficiency.

3) Hemodynamic Instability:

a) Hypertension: (more common)

Causes: • Pain, hypoxia, hypercarbia, or full bladder.
• **Blunting of carotid baroreceptor mechanisms secondary to carotid sinus dysfunction induced by surgical trauma or local anesthetics.**

Complications: • Myocardial infarction and arrhythmias.
• Bleeding at the operative site.
• Intracerebral hemorrhage.

Treatment: maintain postoperative arterial blood pressure at the low normal range by:
• Treatment of the cause.
• If it is due to blunting of carotid baroreceptor reflex, it should be treated by antihypertensive drugs e.g., hydralazine, Na^+ nitroprusside, nitroglycerin, propranolol, esmolol, or labetalol.

b) Hypotension:

Causes: • Hypovolemia and residual effect of anesthetics.
• Myocardial ischemia and cardiac arrhythmias.
• Residual effect of antihypertensive drugs used intraoperatively.
• **Increased sensitivity of the carotid sinus due to exposure of the carotid baroreceptor**

mechanism to higher pressures following removal of the plaque and repair of the stenosis.

Treatment: • Treatment of the cause.
• If it is due to increased sensitivity of the carotid sinus, i.v. fluids and inotropes are given.

4) Respiratory Insufficiency: It is a life threatening condition.

Causes: • Vocal cord paralysis due to traction on **the recurrent laryngeal nerve** requiring immediate reintubation.
• **Neck hematoma,** which needs immediate evacuation.
• **Neck and airway edema** due to venous or lymphatic obstruction or due to the surgical dissection, which causes diffuse lateral and retropharyngeal edema and edema at the supraglottic area. This makes re-intubation and mask ventilation difficult; so, awake intubation is needed (opening of the wound is not effective).
• **Phrenic nerve paralysis** due to cervical plexus block. It only causes respiratory insufficiency if There is severe pulmonary disease or diaphragmatic dysfunction on the other side.

5) Tension Pneumothorax:

It causes respiratory distress, absent breath sounds, and hemodynamic instability. It may occur due to air dissection through the wound and mediastinum to the pleura.

6) Loss of Chemoreceptor Function:

Loss of chemoreceptor function occurs due to **carotid body damage**. There is loss of ventilatory response to hypoxia or hypercarbia with **increased resting $PaCO_2$** by 6 mmHg above the normal. This usually occurs in most patients after carotid endarterectomy and may persist for about **10 months.**
This complication is potentially **very serious** particularly in patients who have had previous contralateral carotid endarterectomy, as the function is lost bilaterally.
Therefore, • Supplemental O_2 should be given to all patients postoperatively.
• Opioids are administered cautiously.

Minimally Invasive Carotid Artery Revascularization (Endovascular Surgical Intervention of Carotid Disease)

It is done for management of carotid artery stenosis by percutaneous interventions such as **carotid angioplasty (balloon inflation) and stenting** via the femoral artery approach or direct puncture of the common carotid artery (less common).

Anesthetic Techniques:

1- Sedation with Monitored Anesthesia Care: is sufficient if the **femoral artery** is used and the patient is **awake.**
2- General Anesthesia: with short acting agents is used if **direct common carotid artery** is used. It allows early recovery for early neurological assessment.

Anesthetic Considerations:

• Proper **monitoring of hemodynamic and neurological** status is essential.
• **Controlling of hypertension** is important to avoid the risk of hematoma formation.
• **Maintenance of adequate perfusion pressures** is particularly important to facilitate collateral blood flow during balloon dilation.
• **Anticholinergics** (atropine or glycopyrrolate) are used to attenuate the baroreceptor response during balloon dilation or stent insertion because profound bradycardia usually occurs with and after dilatation. The aim is to keep heart rate at about 70 beat/min. Some recommend an external pacemaker to be readily available.
• Micro-embolization of atherosclerotic material into the cerebral circulation during the procedure may occur; therefore, some surgeons employ protection devices (balloons or umbrellas) during carotid stenting to reduce embolization of debris into the cerebral circulation.
• **Heparin (bolus and infusion)** is titrated to achieve an activated clotting time (ACT) of 250-300 seconds.

Contraindications to Carotid Angioplasty and Stenting:

1- Intolerance to antiplatelet agents or possibility of open surgery that precludes antiplatelet agents.
2- Aortic arch disease.
3- Abnormal carotid morphology as carotid tortuosity.
4- Carotid concentric calcification, which increases risks of vessel rupture.
5- Heavy thrombus burden and unstable plaque as both increase the risks of embolization.
Still carotid endarterectomy is the gold standard therapy.

Anesthesia for Aortic Surgery

Anatomical Parts of the Aorta and their Significance

The ascending aorta:

It lies between the aortic valve and innominate artery. During surgeries in the ascending aorta, care is taken for **coronaries and aortic valve**.

The arch of the aorta:

It lies between the innominate artery and left subclavian artery. During surgeries in the arch of the aorta, care is taken for **cerebral** circulation.

The descending thoracic aorta:

It lies between the left subclavian artery and the diaphragm. During surgeries in the descending thoracic aorta, care is taken for **spinal and renal** circulation.

The abdominal aorta:

It lies below the diaphragm. During surgeries in the abdominal aorta, care is taken for **renal and spinal** circulation (figure 24-3).

N.B.: Thoracic aorta includes the ascending, arch, and descending thoracic aorta.

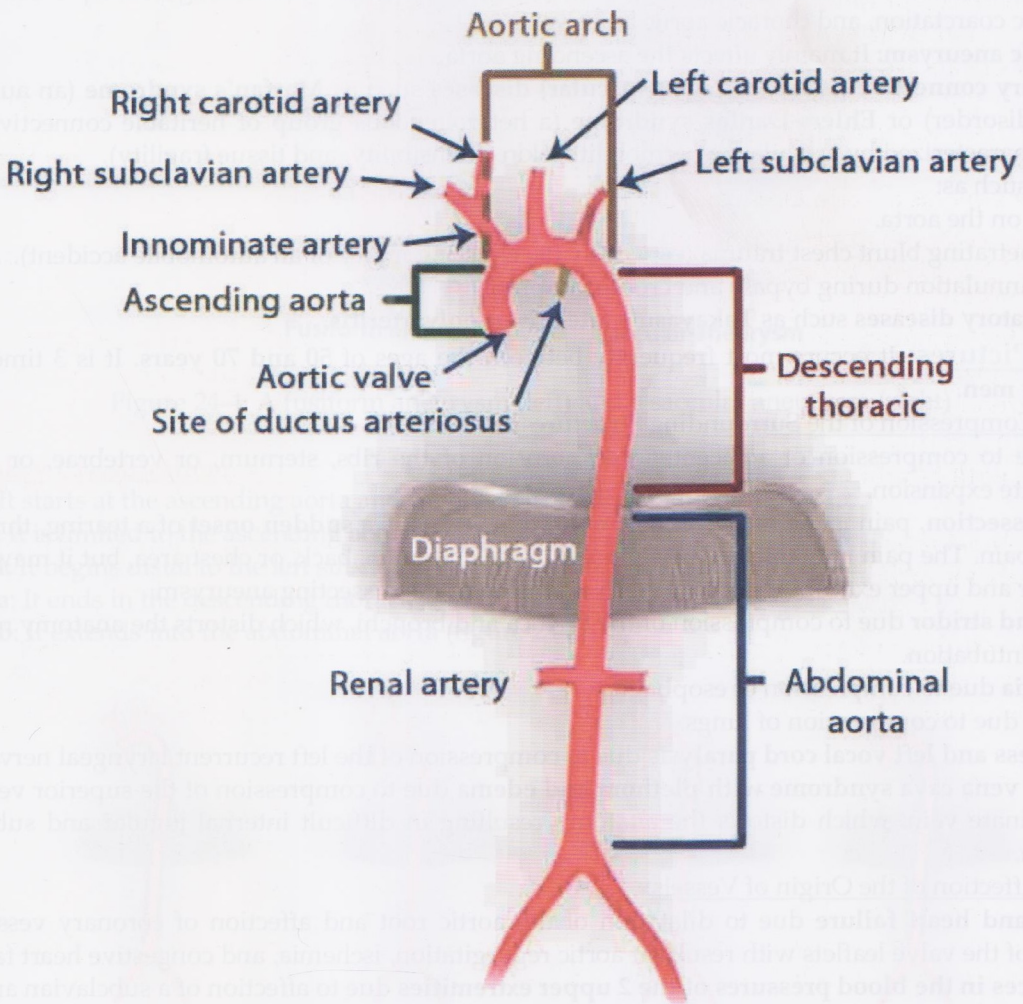


Figure 24-3: Parts of the aorta

Indications of Aortic Surgery:

- Aortic aneurysm and aortic dissection.
- Aortic occlusive disease.
- Aortic trauma.
- Coarctation of the aorta.

A) Aortic Aneurysm and Aortic Dissection

Aortic aneurysm is a dilatation of all three layers of the aorta resulting in a 50% increase in diameter compared to normal.

Aortic dissection is a distinct entity from the aortic aneurysm. It arises from a tear in the intima. Blood surges through the intimal tear into a false channel called the false lumen within the media. Therefore, the hematoma may dissect for variable distances causing no problems or producing one of the following problems:

- dissection that may occlude side branches, or rupture through the adventitia resulting in end-organ failure.
- dissection that may produce aortic valve regurgitation.

Blood in the false lumen can reenter the true lumen anywhere along the course of the dissection.

Causes:

1- Atherosclerosis: It mainly affects the abdominal aorta. **Hypertension** is the main risk factor for dissecting aortic aneurysm.

2- Medial cystic necrosis: It mainly affects the thoracic aorta. **50%** of cases of **bicuspid aortic valve** with cystic degeneration are associated with aortic aneurysm.

Turner's syndrome is associated with multiple cardiovascular anomalies including a bicuspid aortic valve (30%), aortic coarctation, and thoracic aortic aneurysm.

3- Syphilitic aneurysm: It mainly affects the ascending aorta.

4- Hereditary connective tissue (collagen vascular) diseases such as **Marfan's syndrome** (an autosomal dominant disorder) or **Ehlers-Danlos syndrome** (a heterogeneous group of heritable connective tissue disorders characterized by articular hypermobility, skin extensibility, and tissue fragility).

5- Trauma such as:

- surgery on the aorta.
- non-penetrating blunt chest trauma (especially decelerating injury of an automobile accident).
- aortic cannulation during bypass and cross-clamping.

6- Inflammatory diseases such as **Takayasu's arteritis or polyarteritis.**

Clinical Pictures:

It occurs most frequently between the ages of **50 and 70 years**. It is 3 times **more common in men**.

A) Due to Compression of the Surrounding Structures:

1. **Pain** due to compression of adjacent nerves, erosion of the ribs, sternum, or vertebrae, or leakage causing acute expansion.

In aortic dissection, pain is the most frequent symptom. There is **a sudden onset** of a tearing, throbbing, or ripping pain. The pain may initially be confined to the abdomen, back, or chest area, but it may radiate to the lower and upper extremities according to extension of the dissecting aneurysm.

2. **Cough and stridor** due to compression of the trachea and bronchi, which distorts the anatomy resulting in difficult intubation.
3. **Dysphagia** due to compression of esophagus.
4. **Dyspnea** due to compression of lungs.
5. **Hoarseness and left vocal cord paralysis** due to compression of the left recurrent laryngeal nerve.
6. **Superior vena cava syndrome with plethora and edema** due to compression of the superior vena cava and innominate vein, which distorts the anatomy resulting in difficult internal jugular and subclavian cannulation.

B) Due to Affection of the Origin of Vessels:

7. **Angina and heart failure** due to dilatation of the aortic root and affection of coronary vessels and separation of the valve leaflets with resultant aortic regurgitation, ischemia, and congestive heart failure.
8. **Differences in the blood pressures of the 2 upper extremities** due to affection of a subclavian artery.
9. **Renal ischemia** due to affection of renal arteries.
10. **Gastrointestinal ischemia or leg ischemia** due to affection of the abdominal aorta.
11. **Neurological deficits** such as **stroke** (due to occlusion of a carotid artery), **paraparesis, or paraplegia** (due to occlusion of blood supply to spinal cord).

C) Due to Rupture of the Aneurysm:

12. **Hypotension, unconsciousness, and death** may occur due to antegrade dissection and rupture into the pleural space, esophagus, or tracheo-bronchial tree. Retrograde dissection into the sinus of Valsalva at

the root of aorta with rupture into the pericardial space leading to **cardiac tamponade** is the **major cause of death.**

The incidence of rupture increases with increased aneurysmal size.

- In lesions 4-7 cm in diameter, the incidence of rupture is 25%.
- In lesions 7-10 cm in diameter, the incidence of rupture is 45%.
- In lesions > 10 cm in diameter, the incidence of rupture is 60%.

The overall mortality from ruptured aortic aneurysm is 75%.

Classifications

a) According to the Morphology of Aortic Aneurysm:

- **A fusiform aneurysm** is a uniform dilation involving the entire circumference of the aortic wall.
- **A saccular aneurysm** is an eccentric dilation of the aorta that communicates with the main lumen by a variable-sized neck (figure 24-4).

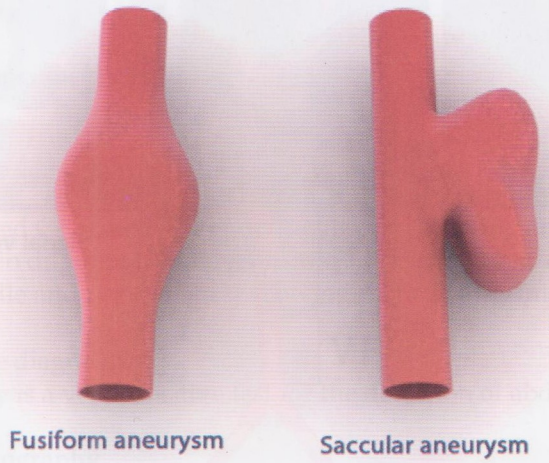


Figure 24-4: A fusiform aneurysm (left) and a saccular aneurysm (right)

b) DeBakey Classification:

Type I: It starts at the ascending aorta and involves the entire length of the aorta.
Type II: It is limited to the ascending aorta.
Type III: It begins distal to the left subclavian artery and extends distally.
IIIa: It ends in the descending thoracic aorta.
IIIb: It extends into the abdominal aorta (figure 24-5).

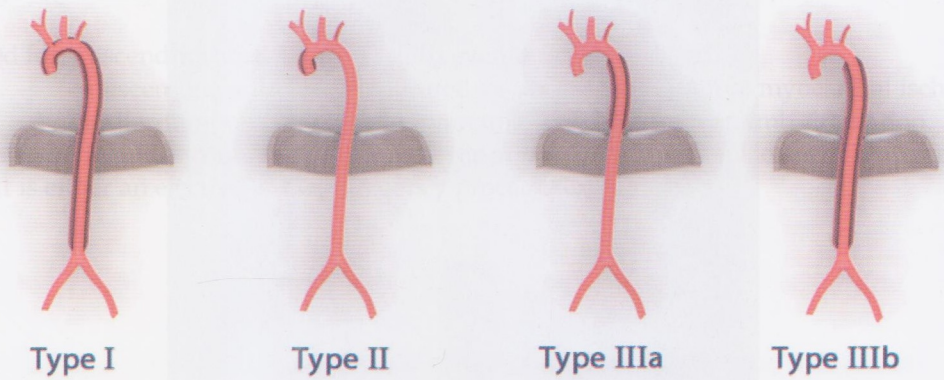


Figure 24-5: DeBakey classification

c) Stanford Classification:

Type A: includes all cases in which the ascending aorta is involved by the dissection, with or without involvement of the arch or descending aorta. It is equivalent to **type I and II DeBakey classification**. It accounts for 50-60% of aortic dissections

Type B: includes all cases in which the ascending aorta is not involved. It is equivalent to **type III DeBakey classification**. It accounts for 40% of aortic dissections.

d) Crawford Classification of Thoraco-abdominal Aneurysms:

Type I: It extends from the proximal descending **thoracic aorta to the upper abdominal aorta**, but it terminates **before the renal arteries**.

Type II: It extends **below the renal arteries**.

Type III: It begins in the **distal half of the descending thoracic aorta** and extends for a variable length into the abdomen.

Type IV: It involves **most of abdominal aorta** (figure 24-6).

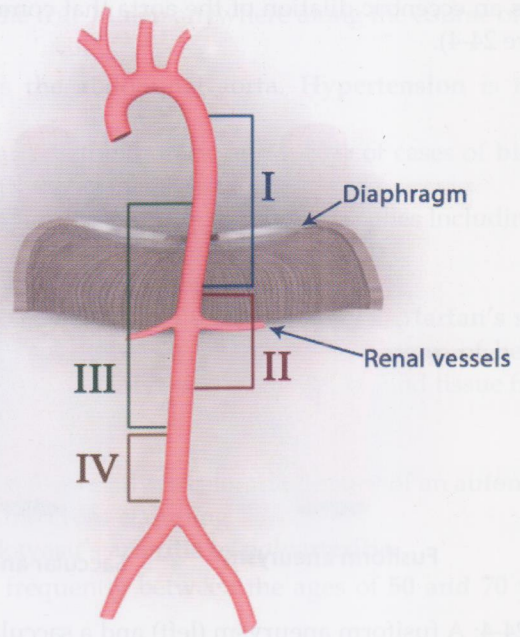


Figure 24-6: Crawford Classification

Investigations:

1- Chest x- ray shows aortic dilation, cardiomegaly, and **mediastinal widening in the thoracic aneurysm**. To evaluate mediastinal widening, **a postero-anterior chest x-ray should be obtained** because antero-posterior views are frequently misleading. If available, prior films should be examined (figure 24-7).

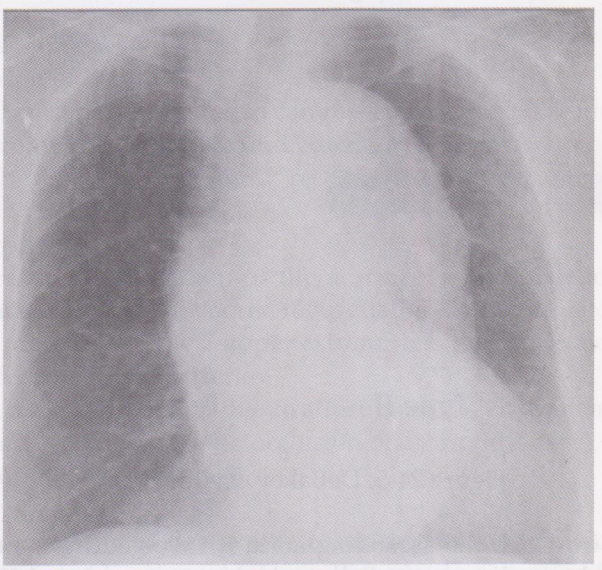


Figure 24-7: Plain chest x-ray PA view showing aneurysmal dilation of the aortic arch and descending aorta

2- ECG shows left axis deviation, left ventricular hypertrophy, ischemic changes, and arrhythmia.
3- CT scan is the **most sensitive test** especially **helical CT** (which provides excellent three-dimensional anatomic details and is particularly useful for evaluating the feasibility of endovascular stent-graft repair of the aneurysm) and **CT with contrast digital subtraction angiography** (figure 24-8).

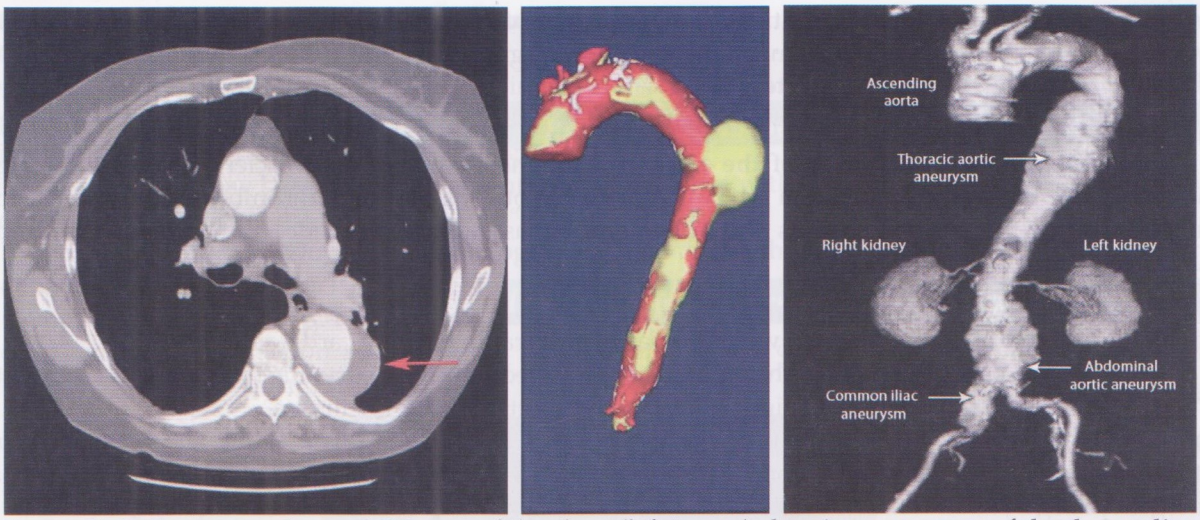


Figure 24-8: Contrast-enhanced CT scan of the chest (left image) showing aneurysm of the descending thoracic aorta (arrow). Two different three-dimensional reconstructions of CT scans of the chest and abdomen (the middle and right images) showing aortic aneurysms in different patients

4- Aortography is the definitive diagnosis.
5- Abdominal ultrasonography is a very sensitive test for the detection of abdominal aortic aneurysms.
6- MRI is also very sensitive.
7- Trans-esophageal echocardiography.

Treatment:

a) Medical Treatment:

- It is indicated for uncomplicated dissection of the descending aorta (i.e., with no end-organ damage) i.e., type B (III). It should be started as soon as the diagnosis is suspected, preferably in the emergency room because: ▫ It may stop the dissection process.
  ▫ It may prevent complications e.g., aortic regurgitation or rupture of affected vessels arising from the aorta.
- Medical treatment includes:
  ▫ Decreasing arterial blood pressure by Na^+ nitroprusside, hydralazine, or methyldopa.
  ▫ Decreasing contractility of the heart by β-blockers e.g., esmolol infusion.

b) Surgical Treatment:

- It is indicated for: ▫ ascending aorta (type A) (I, II) even if uncomplicated.
  ▫ descending aorta, if complicated, as aortic regurgitation, myocardial ischemia, cardiac tamponade, cerebral infarction, and occlusion of limb circulation.
- Surgical treatment includes complete resection of the affected part and replacement by a prosthetic graft (figure 24-9). It is either an elective or an emergency procedure.

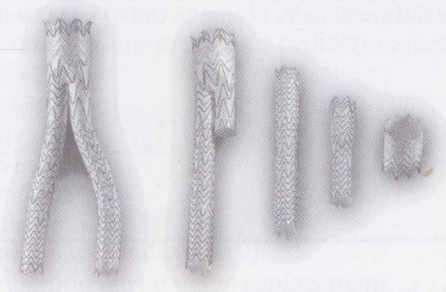


Figure 24-9: Aortic prosthesis

- Elective: if the aneurysm changes rapidly or if the aneurysm diameter is > 4-6 cm.
- Emergency: if the aneurysm ruptures.

• Prognosis:
- In the untreated symptomatic patients, the 5 year survival rate is < 10%. Most patients die from rupture.
- In asymptomatic normotensive patients, longer survival occurs (discovered radiologically).
- In cases with progressive enlargement, there is poor prognosis.
- When it ruptures, the mortality rate is 75-100%.

B) Aortic Occlusive Disease e.g., Leriche's Syndrome

It is **thrombo-embolic obliteration of the aorta**. It is the most common atherosclerotic disease in origin and occurs at the aortic bifurcation as both atherosclerotic plaque and thrombosis cause occlusion. Surgical treatment is needed such as aorto-bifemoral bypass with a synthetic graft. Proximal thrombo-endarterectomy may also be needed.

C) Aortic Trauma (and Aortic Transection)

It is either: • Penetrating such as stab wound or iatrogenic trauma during cardiac surgery.
• Non-penetrating blunt chest trauma such as decelerating injury due to automobile accident or due to falling from a height resulting in dissecting aortic aneurysm.

The most common site of injury is just distal to the left subclavian artery at the site of ligamentum arteriosus. This causes massive hemorrhage (which widens the mediastinum in chest x-ray). It needs an emergency surgery.

D) Coarctation of the Aorta

It is a congenital disease consisting of a discrete, diaphragm-like ridge (a narrowing segment) extending into the aortic lumen. It is more in males.

Coarctation of the aorta is either:

	Infantile (Preductal)	Adult (Postductal)
Site	Coarctation lies **immediately proximal to the left subclavian** artery (i.e., preductal).	Coarctation lies **just distal to the subclavian artery** at the site of the aortic ductal attachment (ligamentum arteriosum) (i.e., postductal).
Clinical Picture	Symptoms appear at **in infanthood**. • **The upper half of the body** is **well perfused** (not cyanotic) due to its good perfusion mainly from the aorta, while **the lower half of the body** is **poorly perfused** (cyanotic) because it is perfused from the pulmonary artery by unoxygenated blood. Later on the lower half of the body becomes better perfused due to presence of the collaterals. • **Blood pressure: no difference** in the systemic blood pressure **in the arms and legs** due to presence of extensive collateral arterial circulation to the distal body through the internal thoracic, intercostal, scapular, and subclavian arteries. • **Murmur: A systolic murmur may be heard on the back** reflecting the collateral blood flow.	Asymptomatic till **adulthood.** • The severity of clinical picture depends on the severity of the narrowing and the extent of collateral circulation that develops to the lower body. • **Blood pressure: Systolic** blood pressure is **increased in arms** (may be associated with headache, dizziness, epistaxis, palpitations) **than legs** (may be associated with weak or absent femoral arterial pulse or with claudications), but **diastolic** blood pressure is **similar in arms and legs**; therefore, wide pulse pressure is present in arms. • **Murmur:** A **harsh systolic ejection** murmur is present along the **left sternal border** and in the **back** particularly over the area of the coarctation.
Complications	• **Left ventricular failure** usually occurs in **the first week of life**.	• **Left ventricular failure later on in life**. • Aortic dissection (especially during pregnancy). • Systemic hypertension. • Premature ischemic heart diseases. • Infective endocarditis. • Cerebral vascular accident due to rupture of intracerebral aneurysm.

Association: It is associated with:
- patent ductus arteriosus (PDA) in 60% of cases,
- ventricular septal defect (VSD) in 30% of cases,

- bicuspid aortic valve (congenital aortic stenosis) in 25% of cases,
- mitral stenosis or mitral regurgitation,
- aneurysms of the circle of Willis, and
- gonadal dysgenesis (Turner's syndrome).

Investigations:

- **ECG**: shows signs of **left ventricular hypertrophy**.
- **Chest x-ray**: shows
  - Increased collateral flow through the intercostal arteries causing **symmetrical notching of the posterior third of the eighth rib**. Notching is not seen in the anterior ribs because the anterior intercostal arteries are not located in costal grooves.
  - The coarctation may be visible as **an indentation of the aorta** with pre-stenotic or post-stenotic dilation of the aorta, producing the reversed "E" or "3" sign.
- **Echocardiography and Doppler ultrasonography:** may show the coarctation and estimate the trans-coarctation pressure gradient.
- **Computed tomography (CT), magnetic resonance imaging (MRI), and contrast aortography:** show precise anatomic information regarding the location, and length of the coarctation and the degree of collateral circulation (figure 24-10).

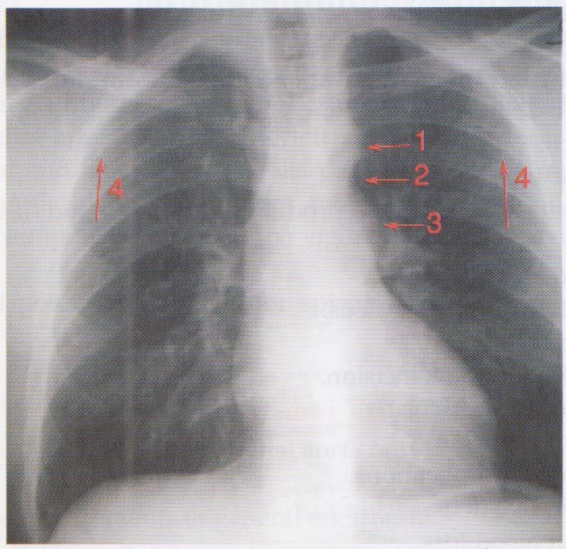


Figure 24-10: Plain chest x-ray, aortic coarctation. The aortic knob (1), the coarctation (2), the post-stenotic dilation of the descending aorta (3) and rib notching caused by the dilated intercostal arteries (4).

Treatment:

- **Antibiotic prophylaxis** against infective endocarditis.
- **Surgical correction** if the trans-coarctation pressure gradient is > 30 mm Hg. During the procedure of repairing aortic coarctation, PDA must be ligated before coarctation is repaired. This causes elimination of the blood flow to the lower half of the body until coarctation is repaired. This causes metabolic acidosis, which requires treatment during this phase of surgery.
- **Balloon dilation**.

Anesthetic Problems and Considerations:

They are **similar to that of thoracic aortic aneurysm** such as cross clamping of the aorta with spinal cord ischemia or kidney ischemia, which needs monitoring and protection (see later).

Anesthetic Management

A) Surgery on the Ascending Aorta

Incision: Median sternotomy.

Anesthetic Problems and Considerations:

1- It needs **cardio-pulmonary bypass** (as cardiac surgery).
2- **Aortic regurgitation** may occur, needing aortic valve replacement.
3- Affection of **coronary vessels** may occur; it may need coronary re-implantation.

4- There are **long aortic cross-clamp times**.
5- There is a great intraoperative **blood loss**; aprotinin may be used.
6- **The left radial artery** is used to monitor invasive blood pressure because clamping of the innominate artery may be done during the procedure. The femoral and dorsalis pedis are suitable alternatives.

B) Surgery on the Arch of Aorta

Incision: Median sternotomy.

Anesthetic Problems and Considerations:

1- It needs **cardio-pulmonary bypass** with **deep hypothermic circulatory arrest.**
2- **Optimum brain protection** is needed because neurological deficits may occur in 3-18% of patients.
Brain protection is achieved by:
- Deep hypothermia 15°C.
- Thiopentone infusion to obtain a flat EEG.
- Methyl prednisone.
- Mannitol.
- Phenytoin.

3- Large intraoperative **blood loss** may occur due to long re-warming periods.

C) Surgery on Thoracic and Abdominal Aorta

Incision:

- **Descending thoracic aorta** by **left thoracotomy ± one lung anesthesia**.
- **Abdominal aorta** by **thoraco-abdominal incision**, which is either:

a- Trans-peritoneal approach:
- Vertical anterior mid-line incision.
- Transverse supra-umbilical incision. It produces less pain and less pulmonary complications postoperatively.

Disadvantages:
- Major fluid and heat loss.
- Prolonged postoperative ileus.

b- Retro-peritoneal approach:
Right lateral decubitus with left flank incision.

Advantages:
- Less wound complications.
- Less fluid requirements.
- Less respiratory complications.
- Less postoperative ileus.
- Less fluid and blood loss.
- Earlier discharge from the hospital.

Anesthetic Management

Preoperative Management

- The same anesthetic management as that of carotid endarterectomy such as assessment of other manifestations of generalized atherosclerosis and other coexisting diseases, preoperative drug therapy, and preoperative investigations.
- Before an elective surgery for the aortic aneurysm, **carotid endarterectomy may be indicated** for patients with transient ischemic attacks or minor strokes with good neurological functions. Asymptomatic carotid bruit is not an indication for delaying aortic surgery because there is no evidence that these patients are at increased risk for strokes during repairing the aortic aneurysm.
- **Two large i.v. cannulas** (14 gauge) are inserted and **many compatible blood units** should be available in the operating room.
- **Risk factors**, which increase mortality, **should be detected**:
  - Preoperative hypotension (systolic blood pressure < 90 mm Hg) increases the risk of mortality by 3 folds.
  - Pre-existing heart diseases including coronary artery disease and congestive heart failure increase the risk of mortality by 2.5-5 folds.
  - Female gender.
  - Age > 80 years.
  - The serum creatinine above 2 mg/dL.

The size of the aneurysm does not appear to affect the risk of mortality.

Premedications:

The same as that of carotid endarterectomy; in addition to the following:

- **Perioperative administration of a single dose of β-blockers** reduces perioperative mortality 50-90%. β-blockers should be **started as soon as** patients are identified to need surgery. β-blockers usually start 7-30 days preoperatively to be continued for at least 30 days postoperatively. Even a single dose β-blocker preoperatively may be useful.
- **Clonidine** may be used in patients with specific contraindications to β-blockade.
- **Prophylactic antibiotics** are indicated especially if vascular grafts are used.

Intraoperative Management

Monitoring:

Monitoring is **the same as carotid endarterectomy (except cerebral function monitoring)** such as:

- ECG: CM_5 lead I configuration or automatic ST segment analysis is used to detect ischemia.
- Urine output.
- Temperature: by an esophageal or tympanic membrane probe.
- Cardiovascular monitors such as pulmonary artery pressure, central venous pressure, cardiac output measurement, and trans-esophageal echocardiography.
- Arterial blood gas analysis.
- Invasive arterial blood pressure: Arterial cannulas are inserted as follows:
  - In abdominal aortic surgery, both radial arteries can be used.
  - In **thoracic aortic surgery, only the right radial artery in addition to femoral or dorsalis pedis** are used. Avoid the left radial artery because the left subclavian artery may be clamped during the surgery. Both right radial and femoral or dorsalis pedis are used to monitor arterial blood pressure above and below the aortic clamp as without monitoring of blood pressure below the clamp, hypertension above the clamp may be treated too vigorously causing severe hypotension in the lower half of the body.
- **Somato-sensory evoked potentials (SSEPs)** for spinal cord function are needed **in thoracic aortic surgery.**

Choice of Anesthesia:

A) Combined General Anesthesia and Lumbar Epidural Block or only Lumbar Epidural Block: (in abdominal aorta only)

Advantages:

- It decreases the anesthetic requirements of general anesthesia.
- It decreases the release of stress hormones to surgery (prolactin, growth hormone, adrenocorticotropic hormone (ACTH), antidiuretic hormone (ADH), cortisol, aldosterone, renin, epinephrine, and norepinephrine.
- It provides postoperative epidural analgesia allowing continuous pain relief, which causes earlier ambulation, faster rehabilitation, and reduction of hospital stay.
- It decreases the hypercoagulability and thrombotic events.
- It does not require airway instrumentation or neuromuscular blockers (if used alone).

Disadvantages:

- Epidural catheters should be inserted before patient's heparinization otherwise epidural hematoma may occur, which causes diagnostic confusion between epidural hematoma and post-ischemic spinal cord injury.
- It decreases the sympathetic tone, which decreases the coronary perfusion.
- It decreases the ability to cough if a high block is applied.
- It does not allow control of ventilation or airway (if used alone).

B) General Anesthesia: (in thoracic and abdominal aortic surgery)

Induction:

- **Smooth induction** is usually indicated as in carotid endarterectomy.
- **In thoracic aortic aneurysm**, the patient lies in the lateral position. **One lung anesthesia by a double lumen tube (Robert Shaw tube) or a Univent bronchial blocker** is used.

Value: 1. **It enhances surgical exposure** by collapsing the nondependent left lung and protects the lung from the trauma of surgical retraction.

2. **Isolation of the right lung** from spillage of blood during initial surgical dissection and

manipulation. It can cause bleeding into bronchi of the nondependent left lung (especially if the patient is heparinized) because the aneurysm is often adherent to adjacent lung tissues.

The technique and **assessment of proper positioning of double lumen tube** are discussed in the chapter of "Thoracic Anesthesia".

Maintenance:

a- If there is good ventricular function, **balanced anesthesia** is needed composed of $O_2 \pm N_2O$, a low concentration a volatile agent, moderate dose fentanyl, a muscle relaxant, and mechanical ventilation.

- **N_2O is avoided** during one lung anesthesia because high O_2 is needed to avoid hypoxia.
- **Low concentrations of a volatile agent:**
  - They may cause cardiac depression; therefore, they should be avoided.
  - They inhibit hypoxic pulmonary vasoconstriction reflex, which may cause hypoxia.
  - Isoflurane > 1% may cause coronary steal, which may cause heart ischemia in patients with coronary artery disease.

b- If there is bad ventricular function, **opioid-based anesthesia** is needed. It has minimal cardiac depression and allows the use of a high FiO_2. To ensure amnesia, the following precautions should be taken:
- High doses of opioids are required to produce amnesia.
- A long acting benzodiazepine as diazepam or lorazepam is used.

Intraoperative Problems:

They include:
- Cross-clamping of the aorta.
- De-clamping of the aorta.
- Increased intraoperative blood and fluid loss.
- Increased heat loss.

1- Cross-Clamping of the Aorta:

Cross-clamping of the aorta is required during the surgery. **Heparin is needed** just before cross-clamping (usually **5000 units**) , which may be reversed after unclamping with protamine 0.5-1 mg/100 units heparin i.v. slowly.

Effects of Cross-Clamping:

a- Proximal to the clamp, **hypertension** (with increased systemic vascular resistance) occurs due to mechanical afterload and due to release of vasoconstrictive mediators (see below), which causes:

- Increased afterload: It increases the cardiac work, which aggravates **heart ischemia, arrhythmias, and left ventricular failure** (i.e., there are increases in central venous pressure "CVP" and pulmonary capillary wedge pressure "PCWP" and a decrease in cardiac index). This can be **assessed by trans-esophageal echocardiography.**
- **Increased intracranial pressure:** It causes **cerebral hemorrhage**.

b- Distal to the clamp, **hypotension** occurs, which causes:

- **Renal ischemia (acute renal tubular necrosis):** It leads to acute renal failure.
- **Spinal cord ischemia (anterior spinal artery syndrome)**: It leads to paraplegia with bowel and bladder dysfunction, but sensation and proprioception are spared (as they are transmitted via the posterior part of the spinal cord).
- **Visceral ischemia.**

Injury to the kidneys, spinal cord, and abdominal viscera is principally due to ischemia, but also due to subsequent reperfusion injury either due to local effects or release of mediators from ischemic and reperfused tissues (distant effects). Mediators include renin-angiotensin-aldosterone system, prostaglandins, catecholamines, O_2 free radicals, and complement cascade.

Management:

The aim is to maintain mean blood pressure **near 100 mm Hg proximal** to the cross-clamp, while maintaining mean blood pressure **>50 mm Hg distal** to the cross-clamp.

The following methods can be used to manage the effects of cross-clamping.

1) Methods Decreasing Proximal Hypertension:

They should be used cautiously because they may decrease mean blood pressure distal to clamp and may decrease renal and spinal cord blood flow in a dose related fashion.

a- Vasodilators: such as nitroglycerin or Na^+ nitroprusside.

b- Inhalational Anesthetics: They decrease arterial blood pressure by cardiac depression and by vaso-dilating effect.

2) Spinal Cord Protection:

Incidence:

Spinal cord ischemia ranges from 0.2% after elective infrarenal abdominal aortic aneurysm repair to 8% in elective thoracic aortic aneurysm repair up to 40% in the setting of acute aortic dissection or rupture involving the descending thoracic aorta.

Monitoring of Spinal Cord:

- Monitoring is done by **somato-sensory evoked potentials (SSEPs)** as ischemia of the spinal cord increases the latency and/or decreases the amplitude as the following:
  - 4 min after aortic cross-clamping, the latency increases.
  - 7 min after aortic cross-clamping, cessation of spinal cord conduction occurs.
  - 47 min after distal aortic reperfusion, spinal cord conduction starts to return.
  - Within 24 hours postoperatively, spinal cord conduction returns to normal.
- During thoracic aortic surgery, SSEPs remain stable, if the **distal aortic pressure is maintained at >50-60 mm Hg,** and at lower pressures, SSEPs disappear gradually.
- **Postoperative paraplegia** has been reported despite normal intraoperative SSEPs. This suggests that SSEPs monitoring may fail to reflect spinal cord dysfunction on two conditions:
  - If the insult does not involve the dorsal column (sensory). SSEPs are not sensitive as they detect the posterior column function (transmitting sensory) and do not detect anterior column (transmitting motor). Anterior spinal cord function is assessed by motor evoked potentials, which impractical since it prohibits use of neuro-muscular blocking drugs.
  - If the insult does involve the dorsal column, but is not of sufficient magnitude to affect the SSEPs.

N.B.: **Blood Supply of the Spinal Cord:**

The spinal cord is supplied by a single anterior spinal artery (it supplies 75% of spinal cord) and two posterior longitudinal arteries (they supply 25% of spinal cord). These arteries are supplied by six to eight paired radicular arteries arising from the vertebral arteries and the aorta at each dermatomal level. At the lumbo-sacral region, at the level of the diaphragm, one of the intercostal arteries called **Arteria Radicularis Magna (or artery of Adamkiewicz)**, which is the largest and most important artery. This artery arises at the level of
- T_9-T_{12} in 60% of patients.
- T_5-T_8 in 15% of patients.
- L_1 in 15% of patients.
- L_2 in 10% of patients.

This artery may be damaged when the thoracic aorta is cross-clamped as its origin may be unknown. The blood supply to the spinal cord may be seriously compromised causing paraplegia.

The diameter of the anterior spinal artery above the entry of Arteria Radicularis Magna artery is smaller (the resistance is higher) than below it. Therefore, the distal aortic perfusion, during thoracic cross clamping, by a bypass or shunt can protect the spinal cord below, but not above the Arteria Radicularis Magna. Paraplegia still occurs in 2-15% of patients with distal aortic perfusion (figure 24-11).

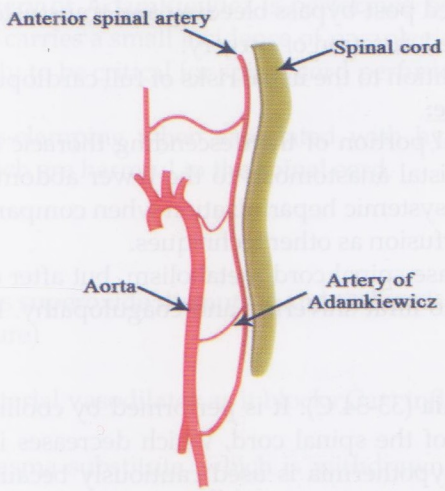


Figure 24-11: Blood supply of the spinal cord

Collateral Network Concept:

This is a recent concept about the blood supply of spinal cord.

1. There is an axial network of small arteries in the spinal canal, in the peri-vertebral tissues, and in the para-spinous muscles that anastomose with one another and with the nutrient arteries of the spinal cord.
2. Inputs into this network include not only the segmental vessels (as described above) but also the subclavian arteries and the hypogastric arteries and their branches.
3. This network can increase cord nutrient flow from one source when another is reduced. Contrariwise, cord nutrient flow can be reduced if an alternate low resistance pathway is opened; that is, steal can occur. Examples of steal include back bleeding of intercostals into an open excluded aortic segment or unperfused iliac or visceral vessels secondary to aortic cross-clamping, and pharmacologically induced arterio-venous shunting such as that resulting from use of nitroprusside.

Management: Spinal cord injury can be avoided by:

1- Decreasing the time of clamping to be < 30 min, which is usually tolerated, but if the time of clamping is > 30 min, the risk of spinal cord ischemia is significant and techniques for spinal cord protection are indicated.

2- Decreasing the complexity of surgical repair and dissection as possible, this is out of our control.

3- Partial Cardio-Pulmonary Bypass:

- It is either:
  - Partial left heart bypass (left atrium-to-femoral artery): The blood is drained from the left atrium to a reservoir and then pushed by a roller pump to the femoral artery.
  - Femoral venoarterial bypass: The blood is drained from the femoral vein to a pump oxygenator and then pushed by a roller pump to the femoral artery.
- **Systemic heparinization is needed**, which increases the blood loss; therefore, some authors avoid the partial cardio-pulmonary bypass
- **Regulation of blood flow through extra-corporeal circuits should be adjusted to provide**:
  - **Systolic blood pressure above the clamp at 100- 150 mm Hg (or 20 mm Hg above the pre- cross).**
  - **Arterial blood pressure below the clamp at 40- 60 mm Hg** (20- 40 mL/kg/min) in order to perfuse the kidneys and the spinal cord, but venous return to the heart is decreased so that the fall in the blood pressure to a very low level above the clamp may lead to hypoperfusion to the heart and brain. Therefore, volume should be added to increase the venous return.

4- Temporary Shunting Technique:

- A shunt is done **from the left ventricular apex or proximal aorta to the distal aorta or femoral artery. Systemic heparinization is not needed** because heparin bonded or coated tubes are used. Blood flow through the shunt cannot be regulated or controlled.

5- Cardio-Pulmonary Bypass with Deep Hypothermic Circulatory Arrest:

Advantages:
- It can protect the spinal cord and kidneys.
- It provides a bloodless field.
- It avoids the hemodynamic changes occurring with cross-clamping.

Disadvantages:
- There is increased post-bypass bleeding and transfusion need.
- There is increased duration of surgery.
- These are in addition to the usual risks of full cardiopulmonary bypass.

6- The Clamp and Sew Technique:

It involves clamping the proximal portion of the descending thoracic aorta and replacing the aneurysm with a graft (figure 24-12). The distal anastomosis to the lower abdominal aorta is performed without a clamp. This technique avoids full systemic heparinization when compared to other techniques, but it does not support distal or collateral perfusion as other techniques.

7- Hypothermia: is used to decrease spinal cord metabolism, but after completing all anastomoses, effort is made to warm-up the patient to limit shivering and coagulopathy. Hypothermia is either systemic or local:

a- Systemic Hypothermia:

i) Systemic Mild Hypothermia (33-34° C): It is performed by cooling blankets, and cold i.v. fluids. It decreases the metabolic rate of the spinal cord, which decreases ischemic injury. Precise control of temperature is difficult; so, hypothermia is used cautiously because temperatures < 32° C make the heart more irritable resulting in ventricular arrhythmias.

ii) Systemic Profound Hypothermia (15-19° C): It causes circulatory arrest. It is used in selected patients: ▫ who require extensive aortic resections or

▫ who are at substantial risk of development of spinal cord injury.

b- Regional Spinal Cord Hypothermia:

It is done by epidural cooling as an epidural catheter is inserted between T_{11-12}. A subarachnoid thermistor catheter is placed at L_{3-4}. Thirty minutes before aortic cross-clamping, iced (4° C) saline solution is infused into the epidural space via the epidural catheter till the cerebrospinal fluid (CSF) temperature reaches 25° C. The infusion is adjusted to maintain this temperature until the aorta is de-clamped. Subarachnoid catheter is also used to measure CSF pressure or to provide CSF drainage.

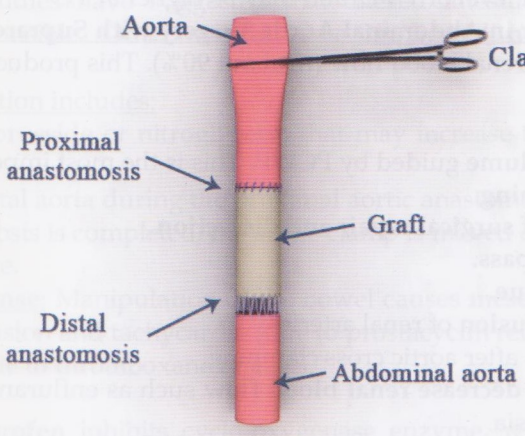


Figure 24-12: The clamp and sew technique

8- CSF Drainage:

• Spinal cord perfusion pressure = mean arterial blood pressure – CSF pressure

Therefore, reduction of the CSF pressure improves the spinal perfusion pressure.

• CSF drainage is performed to make CSF pressure between 10-12 mm Hg.

• Cross clamping the thoracic aorta is associated with an increase in CSF pressure about 3-5 mm Hg, which decreases spinal cord perfusion pressure. Presumably, intracranial hypertension due to systemic hypertension above the clamp produces redistribution of blood volume and engorgement of the intracranial compartment (intracranial hypervolemia). This results in redistribution of CSF into the spinal fluid space and a decrease in the compliance of the spinal fluid space. Therefore, CSF drainage might also increase the spinal cord blood flow.

• Recent studies do not show that CSF drainage is beneficial in preventing paraplegia and may cause intracerebral hemorrhage due to excessive intracerebral fluid shifts with tearing of cerebral bridging.

9- Re-implantation of the intercostal and lumbar arteries:

• Preoperative identification of **artery of Adamkiewicz** is performed by **selective angiography** of intercostal arteries (this procedure itself carries a small incidence of paraplegia).

• Arteries identified intraoperatively to be critical for spinal cord perfusion are re-implanted or preserved.

10- Avoiding Hyperglycemia:

Presence of ischemia due to cross-clamping when associated with hyperglycemia produces anaerobic metabolism and lactic acidosis, which are harmful to the spinal cord.

11- Neuro-protective Agents:

• Steroids.

• Barbiturates

• Free O_2 radical scavengers such as superoxide dismutase and tirilazad.

• Mannitol (it decreases CSF pressure)

• Ca^{++} channel blockers.

• Intrathecal papaverine; it is an arterial vasodilator as it blocks Ca^{++} influx into cells and it also acts as an indirect O_2 free radical scavenger.

• Fluosol DA (it is an artificial plasma substitute, which is withdrawn from the market due to allergic effects).

• NMDA receptor antagonists.

• Opioid antagonists e.g., naloxone.

- Magnesium sulphate: ▫ It stimulates alkaline phosphate and pyrophosphatase.
  ▫ It is a NMDA channel blocker decreasing Ca^{++} influx.
  ▫ It acts as a vasodilator.
  ▫ It produces a muscular relaxant effect.

Magnesium sulphate is given i.v. at a rate of 40 mmol (10grams) in 24 hours followed by 24 mmol/day for 2-5 days for elective cases or 8 mmol (2gm) in 10 ml of D5W over 10min followed by 20 mmol (5 gm) in 500 ml D_5W over 3-12 hours for emergency cases.

3) Renal Protection:

Renal arteries arise from aorta at level of T_{10}-L_1 and may be higher at T_8.

a- In Thoracic Aortic Surgery or in Abdominal Aortic Surgery with Suprarenal Aortic Cross Clamping:

There is a profound decrease in renal blood flow (to about 90%). This produces irreversible renal ischemia resulting in acute renal failure.

Renal protection is done by:

1- Maintaining **intravascular volume** guided by PCWP. This is the most important factor.
2- Decreasing the time of clamping.
3- Decreasing the complexity of surgical repair and dissection.
4- Partial cardio-pulmonary bypass.
5- Temporary shunting technique.
6- Hypothermia: with cold perfusion of renal arteries.
7- Avoiding distal hypotension after aortic cross clamping.
8- Avoiding anesthetics which decrease renal blood flow such as enflurane, isoflurane, desflurane, and hypotension of regional anesthesia.
9- Selective Perfusion: It allows arterial flow via the renal, mesenteric, and splanchnic circulation. Small special catheters are used to cannulate the mesenteric, celiac, and renal arteries. The flow is derived from the upper aorta into these arteries by the centrifugal pump to decrease the ischemic time of the gut and kidneys.
10- Renal protective agents: None of them provides good renal protection.

- **Mannitol**: Values: ▫ It produces osmotic diuresis.
  ▫ It causes renal artery vasodilation by increasing renal prostaglandins (PGs), which increase renal blood flow and redistribute it to the cortex.
  ▫ It acts as a renin antagonist.
  ▫ It increases glomerular filtration rate (GFR) (independent of increased renal blood flow).
  ▫ It flushes the tubular debris away from the nephrons by increasing the velocity of the tubular fluid. This relieves tubular obstruction.
  ▫ It acts as a free O_2 radical scavenger.

- **Furosemide**: Values: ▫ It produces natriuresis.
  ▫ It produces renal artery vasodilation by increasing PGE_1.
- **Dopamine** low dose 2-4 µg/kg/min; values: ▫ It inhibits tubular transport of Na^{++}.
  ▫ It increases renal blood flow and GFR.
  ▫ It redistributes intra-renal blood flow.

Actually, the renal protective effect of dopamine is unproved clinically.

- Experimental renal protective agents:
  ▫ Ca^{++} channel blockers.
  ▫ Fenoldopam (selective D_1 agonist); it has renoprotective action especially in high risk patients during vascular and cardiac surgeries.
  ▫ Free O_2 radical scavengers (superoxide dismutase).
  ▫ PGE_1.
  ▫ Phosphodiesterase inhibitors.
  ▫ Angiotensin converting enzyme inhibitors.
  ▫ Epidermal growth factor.

b- In Abdominal Aortic Surgery with Infra-Renal Aortic Cross-Clamping:

Renal blood flow decreases to a lesser extent (about 40%), but cross-clamping also decreases cardiac output, which may be the cause of renal ischemia resulting in acute renal failure in 5% of cases.

Renal protection is done by:

1- Maintenance of cardiac output that is the primary goal e.g., by alteration in anesthetic depth or infusions of vasodilators.

2- Mannitol, furosemide, and dopamine as above.

4) Gastrointestinal and Mesenteric Protections (and Complications):

a- Visceral ischemia: supra-renal cross-clamping of the aorta causes a marked decrease in inferior mesenteric blood flow (which arises from the aorta at the level L_1-L_5), while infra-renal cross-clamping causes a slight decrease in inferior mesenteric blood flow. This results in visceral ischemia, which has been implicated as an important cause of **coagulopathy**. Although the exact mechanism of coagulopathy remains uncertain, some studies have suggested that altered intestinal permeability with **bacterial translocation** may be responsible. Other studies have implicated **hepatic ischemia** with primary fibrinolysis.

Strategy of mesenteric protection includes:

- **Vasodilators** such as nitroprusside or nitroglycerin that may increase the arterio-venous shunts in the splanchnic bed.
- Elective perfusion of the distal aorta during the proximal aortic anastomosis.
- Once the proximal anastomosis is completed, the aortic clamp is moved distally to the infra-renal aorta.
- **Selective perfusion** as above.

b- Mesenteric traction response: Manipulation of the bowel causes **mesenteric traction response,** which produces: • Initially, hypotension and tachycardia (due to prostacyclin release). It lasts for 20-30 min.
then • Hypertension (due to thromboxane release).

Prevention:

- Pretreatment with **ibuprofen** inhibits cyclo-oxygenase enzyme, which decreases prostacyclin; 12 mg/kg oral 1- 1.5 hour preoperatively or 800 mg/6 hour for 3 doses.
- **Ketorolac** inhibits cyclo-oxygenase enzyme, which decreases prostacyclin.

Treatment: • I.v. Fluids.
• Vasoconstrictors.
• Diphenhydramine.

2- De-clamping of the Aorta:

Effects: **De-clamping shock or release hypotension** occurs due to:

1- Sudden decrease in the afterload due to pooling and redistribution of blood in reperfused tissues (lower limbs).

2- Reperfusion of lower parts of the body allowing acid metabolites to enter the circulation. This causes vasodilation and metabolic acidosis. Some authors advocate that metabolic acidosis has a little effect.

3- Bleeding is maximal at this time as the adequacy of the vascular anastomosis is tested leading to severe hypotension.

4- Hypovolemia.

5- Reactive hyperemia.

6- Release of vasoactive substances and myocardial depressant metabolites from ischemic tissues. These metabolites may also increase pulmonary capillary permeability resulting in pulmonary edema.

7- Allergic reaction to graft materials.

8- Hypoxia-mediated vasodilation: After cross-clamping release, a large volume of desaturated blood returns to the heart from hypoperfused tissues below the cross-clamp. However, the transit time through the pulmonary circulation may be inadequate for hemoglobin to be fully saturated. The result is temporary systemic hypoxemia.

Management:

1- **Relative hypervolemia** is allowed during or just before de-clamping by fluid infusion to produce CVP 10- 12 cm H_2O or PCWP 15 mm Hg i.e., elevate CVP and PCWP just above normal values.

2- **Decrease the depth of anesthesia.**

3- **Gradual de-clamping** is recommended. If severe hypotension is present, ask the surgeon to constrict the aorta by his hand or re-clamp again. Gradual de-clamping allows time for more fluid loading and to slow the washout of the vasoactive and cardio-depressant mediators from ischemic tissues.

4- **Discontinue vasodilators and give vasopressors** e.g., phenylephrine 0.1 mg increments or calcium chloride 300-500 mg that can offset the negative inotropic/chronotropic effects of an acute potassium and acid load.

5- **Correct metabolic acidosis** by $NaHCO_3$ if present.

6- **Superoxide dismutase** (a free radical scavenger) can be used.

If hypotension is persistent in spite of the above measures, hypotension is mostly due to left ventricular dysfunction or failure due to myocardial ischemia or continued hemorrhage. To differentiate between them, measure the filling pressures as left ventricular dysfunction with/without myocardial ischemia is associated with hypotension and increased filling pressure, but continued hemorrhage is associated with hypotension with decreased filling pressure.

3- Increased Intraoperative Blood and Fluid Loss:

Therefore,

1- Increase intraoperative fluid therapy to 10-12 ml/kg/h because there are excessive wound and 3rd space losses especially in abdominal aortic surgery.
2- PCWP (more sensitive) and CVP monitor should be used.
3- Adequate venous access must be secured.
4- Blood-scavenging device (cell saver) for auto-transfusion is beneficial.
5- Prophylactic aprotinin may be helpful.

4- Increased Heat Loss:

Cause: • The patients are geriatric with low metabolic rates.
• There is extensive surgical exposure (of the bowel outside the abdomen) especially in abdominal aortic surgery.

Management:

- Warming of infused fluids.
- Warming and humidification of anesthetic gases.
- Using a heat blanket.
- Wrapping the bowel in a clear plastic bag.
- Humid warm ambient atmosphere in operating room.

Extubation and Recovery:

- In short cases with minimal fluid shifts, the patient can be extubated immediately.
- In long cases with great fluid shifts, the patient can be extubated after fulfilling the criteria of extubation.
  - A stable hemodynamic state.
  - A vital capacity > 15 mL/kg.
  - Maximum negative inspiratory force < - 20 cm H_2O.
  - pH > 7.3.
  - PaO_2 > 60 mm Hg at FiO_2 < 50%.
  - $PaCO_2$ < 50 mm Hg.

Postoperative Management and Intensive Care Considerations

The patients are usually transferred to an **intensive care unit.**

Continuing Monitoring of the cardiovascular system especially CVP for the 1st 12-24 hours because:

- Vasodilation may occur in response to increased body temperature.
- Blood oozing may continue from the anastomosis.

Postoperative Complications:

1- Hypertension, hypotension, arrhythmias, and heart infarction.
2- Hemorrhage.
3- Gastrointestinal complications.
4- Flaccid paraplegia: (especially in thoracic aortic surgery)

It is the most serious complication. Its incidence is increased in ruptured aneurysms. It occurs due to intraoperative decrease in spinal cord blood flow. Paraplegia **usually** occurs **in the immediate postoperative period. Delayed** appearance of postoperative **paraplegia (12 hours to 21 days postoperatively)** has been associated **with postoperative hypotension** in patients with severe atherosclerotic disease in whom marginally adequate collateral circulation to the spinal cord is present.

Factors causing paraplegia: • Long duration of aortic clamping.
• Resection of long aortic segment.
• Clamping or damage of radicular branches.
• Prolonged hypotension.
• Atherosclerosis of the cord vessels and preexisting aortic disease.

- Compression of the intercostal arteries by a dissecting aneurysm.
- Subclavian steal.

The classic picture is **an anterior spinal artery syndrome**. There is loss of motor functions and pinprick sensations, but with preservation of vibration and proprioception.

5- Renal failure.

6- Respiratory failure occurs especially with trans-peritoneal approach with upper abdominal incisions. To decrease the postoperative respiratory impairment the following precautions should be taken:

- Good postoperative analgesia.
- Early ambulation.

Causes of respiratory failure:

- Pulmonary contusions.
- Injury of the left phrenic nerve or left recurrent laryngeal nerve.
- Preexisting pulmonary diseases.
- The use of one-lung ventilation.

7- A hyper-coagulable state, which causes thrombosis of the vessels. It is decreased by combined epidural and general anesthesia.

Postoperative Analgesia:

Postoperative analgesia is important especially with postero-lateral thoracotomy because this incision produces great pain as major muscles are transected and ribs are removed. Pain can be managed by:

1- Neuraxial (spinal or epidural opioids) with/without local anesthetics. Some authors recommend the use of opioids alone because they do not affect the muscle and thus avoid masking of the anterior spinal artery syndrome.

2- Systemic opioids.

3- Non-steroidal anti-inflammatory drugs (NSAIDs).

4- Transcutaneous electrical nerve stimulation (TENS).

Emergency Aortic Surgery

Emergency aortic surgery is usually indicated in ruptured abdominal aortic aneurysm.

Anesthetic Problems and Considerations:

Besides **the anesthetic measures of abdominal aneurysm repair**, the following considerations should be in mind:

1- Clinical picture:

- **The classic triad** (**hypotension, back pain, and a pulsatile abdominal mass**) is present only in approximately **50% of patients** who have a ruptured abdominal aortic aneurysm.
- **Hypovolemic shock** may be **present, but in some cases, blood pressure may be maintained** due to clotting, tamponade effect of the retro-peritoneum, and the tone of abdominal muscles. Death is likely unless the rupture is contained in the retroperitoneal space. Therefore, when a muscle relaxant is used sudden drop of blood pressure may occur.

2- If there is doubt, diagnosis is confirmed by ultrasound or CT scan if time is available.

3- Euvolemic resuscitation may be delayed until the aortic rupture is surgically controlled in the operating room (i.e., allow **permissive hypotension**) because euvolemic resuscitation and the resultant increase in blood pressure without surgical control of bleeding may lead to loss of retro-peritoneal tamponade, further bleeding, hypotension, and death. In the operating room, **massive blood transfusion** is usually needed.

4- Induction of anesthesia is only done in the operating room with the **surgeons scrubbed**, surgical preparation completed, drapes on, blood available in the theater and checked, and the patient is ready for surgery. **Rapid sequence induction** is appropriate with preoxygenation and suxamethonium (unlike in elective aortic aneurysm repair where smooth induction is chosen). Suitable induction agents include etomidate, fentanyl, or ketamine. As soon as the endotracheal tube is confirmed, the surgeons can start laparotomy immediately and aortic cross-clamping is performed as soon as possible.

5- Hypotension usually occurs after induction. It can be treated by rapid infusion of i.v. fluids and blood and small doses of vasopressors/inotropes.

6- Recovery and extubation: Do not attempt to extubate at the conclusion of surgery. **A postoperative period of ventilation in the intensive care unit is essential** to allow correction of biochemical and hematological abnormalities.

7- The **prognosis is poor**. The mortality in this emergency surgery is high due to:

- No preoperative preparation.
- No proper management of coexisting diseases.
- Severe hypotension resulting in impairment of renal, cardiac, cerebral, and hepatic function.
- Postoperative jaundice due to hemolysis of damaged red blood cells in the circulation and in a large retro-peritoneal hematoma.

The overall mortality from ruptured abdominal aortic aneurysm is 75%.

Minimally Invasive Aortic Surgeries include:

A) Endo-luminal Aortic Stent-Graft Surgery (Endovascular Approach)

- The procedure involves placing endovascular stent-graft devices into the aorta to exclude the aneurysm sac from the high pressure of systemic circulation, thereby allowing for sac thrombosis around the stent and avoiding its rupture. It can be done for both elective and emergent cases.
- The procedure is usually performed in the radiological suite in which the anesthesiologists must ensure that anesthetic facilities for high-risk patients are adequate.

Indications of Endovascular Repair:

1- The proximal aneurysm neck must be at least 15 cm in length.
2- The maximum aneurysm diameter should be no longer than the largest available endograft.
3- The distal attachment site must also be non-aneurysmal and of sufficient length to accommodate the graft i.e., there must be an adequate fixation zone between the distal end of the aneurysm and the renal arteries (in abdominal aortic aneurysm) or the celiac vessels (in thoracic aneurysm) to allow adequate fixation of the stent (figure 24-13).
4- There must be at least one large, straight iliac artery, which can be used as a conduit for graft delivery.

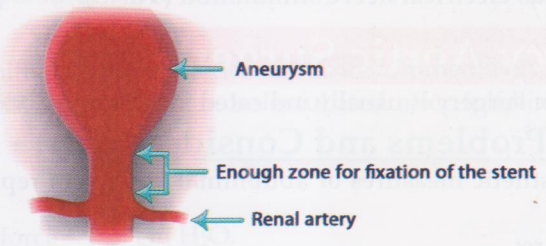


Figure 24-13: The distal end of the graft

Advantages:

- The procedure is less invasive.
- Local or regional anesthesia may be used.
- Less wound complications are expected and thoracotomy is avoided (in thoracic aortic surgery).
- Less blood and fluid loss is expected.
- Less hemodynamic and metabolic effects occur with less stress response.
- The aorta is only briefly occluded.
- Less respiratory complications are encountered.
- Earlier extubation is usually done.
- Early ambulation can be done.
- Earlier discharge from the intensive care unit and hospital with reduced costs is allowed.
- Lower mortality rates.

Surgical Procedure:

- A small incision is made over the femoral or iliac artery, where a puncture is made and a guide wire is inserted and advanced into the thoracic aorta, over which an introducer is inserted under radiological guidance. Once the stent-graft is properly positioned, it is then deployed. Finally, a global angiography is performed to check for any endoleaks with additional balloon inflation or cuff extension being performed as necessary to complete sealing.
- For aortic dissections, the endoluminal graft is deployed in the true channel, covering the proximal dissection entry site. Intraoperative trans-esophageal echocardiography is extremely helpful in confirming exclusion of the false channel.

Anesthetic Considerations and Problems:

The preoperative assessment and preparation are the same as that of open repair.

Monitors:

In addition to the standard monitors, the following monitors are essential:

- Central venous pressure.
- Invasive intra-arterial blood pressure.

Choice of Anesthesia: One of the following methods can be used:

a- Regional Anesthesia:

Regional anesthesia such as **continuous spinal, single shot spinal, epidural, or local infiltration** (in the area of incision) with **minimal sedation** and **monitored anesthesia care (MAC)** is common. It allows early postoperative ambulation.

b- General Anesthesia:

It can be used. It allows securing the airway if the aneurysm ruptures.
Conversion to open surgery may be required.

Complications (and Disadvantages) of Endovascular Repair

1- Endoleak:

- It is the **most common complication**. It is defined as persistent blood flow outside the wall of the stent graft into the aneurysmal sac. This exposes the weak aneurysm wall to continued blood flow that may lead to rupture. Therefore, any increase in the sized of the aneurysm sac warrants immediate interventions.
- There is a grading system that classifies the endoleaks:

Grade	Description
Grade I	**High pressure, high flow leak** adjacent to a stent that is not sealing the sac from the systemic circulation i.e., there is a direct communication between the aneurysm sac and aortic blood flow.
Grade II	**High pressure, low flow** due to arterial branches, which have been excluded by the position of the stent (such as inferior mesenteric and lumbar arteries).
Grade III	Resulting from a failure within the stent itself.

2- Problems with Percutaneous Arterial Access:

- Percutaneous arterial access may not be feasible in obese patients or patients who have had previous groin procedures or surgery. This necessitates open groin access and arteriotomy. Aggressive attempts may lead to **retroperitoneal hematoma** and significant morbidity and mortality.
- Because larger devices are necessary to accommodate the diameter of thoracic aorta, arterial access is more problematic.

3- Problems during Removal of the Introducer and Sheath upon Completion of the Surgery:

- This may cause a **tear in the internal iliac artery**. This tear may not be readily apparent because the bleeding is retroperitoneal and the anesthesiologist may be the first to identify a problem with the onset of profound hypotension.

4- Balloon Malfunction (Inflation):

- It may severely **decrease distal blood flow** acting in the same manner as an aortic cross clamp. Newer systems deploy quickly with less fluctuations in hemodynamics.

5- Distal Migration or Mal-positioning of the Stent-Graft:

- It is common especially with **old devices which are balloon-based**. Distal migration occurs due to forward aortic blood flow especially in thoracic endovascular repair. Distal migration may cause:
  - **Partial obstruction of renal ostia**, which may cause **renal dysfunction** after long period after surgery
  - **Complete obstruction of renal ostia** (and may be due to thrombosis); this may cause **renal infarction**. It is very rare.
  - Obstruction of other major branches resulting in **mesenteric or pelvic ischemia or infarction**.
  - **Incomplete aneurysm exclusion**.

Therefore, induced hypotension may be used to reduce device migration and some physicians temporarily induce asystole by administering high-dose adenosine.

• Newer generation endografts are either thermally- or mechanically-activated during proximal graft deployment. Therefore, they tend not to migrate and induced hypotension is generally not required.

6- Hypotension after Graft Placement:

• It may be due to ▫ aortic rupture,
▫ allergic reaction to i.v. contrast dye,
▫ adenosine side effect or
▫ sympathetic nerve blockade if regional anesthesia is used.

Therefore, large bore i.v. cannulas, central venous access, arterial line, vasoactive agents, and rapid infusion devices should be ready available.

7- Contrast-induced Nephropathy:

• A significant dye load may be given during angiography that may affect **renal function**.

Therefore, **renal protection** is advised by adequate preoperative hydration, n-acetyl cysteine (a free radical scavenger), and sodium bicarbonate.

8- Aneurysm Rupture:

It is a rare catastrophic complication that may occur due to endotension which is elevated pressure within the aneurysm sac unrelated to endoleak.

It necessitates immediate exploration and direct surgical control with wide bore cannulas and rapid infusion devices that should be available.

9- Spinal Cord Ischemia and Paraplegia:

The incidence is similar to that of open repair especially in thoracic aortic endovascular repair when longer grafts are used because a greater number of intercostal arteries are excluded despite the absence of aortic cross-clamping.

10- Post-implantation Syndrome:

It is characterized by fever, elevated C-reactive protein levels, and leukocytosis. It is usually mild and self-limiting lasting from 2 to 10 days. It is treated with non-steroidal anti-inflammatory drugs.

Most of the complications may necessitate immediate exploration and conversion to open surgery.

B) Laparoscopic Management of Abdominal Aortic Surgery

Recently, hand-assisted, robotic-assisted, and totally laparoscopic abdominal aneurysm repair is done. Also, combined endovascular and laparoscopic approach is performed.

Q: Discuss organ protection in aortic aneurysm anesthesia?

A: The following organs should be protected; brain protection, spinal cord protection, heart protection, and renal protection.

Q: Discuss organ protection?

A: In addition to the above, lung protective strategy should be discussed.

Peripheral Arterial Surgeries and Diseases

a- Acute Peripheral Arterial Occlusive Disease (Embolism)

Cause: The main cause is embolism, which may be originating from:

- Mural thrombosis from **left ventricular infarction**.
- **Fibrillating** left atrium.
- **Prosthetic valve** disease.
- Vegetations of **infective endocarditis**.
- Left atrial **myxoma**.
- **Atheromatous lesions** in the abdominal aorta or ilio-femoral artery.

Clinical Picture: Sudden pain, skin color and temperature changes below the level of arterial occlusion.

Treatment: • Surgical embolectomy.
• Heparin therapy (i.v. or local).

Anesthetic Management:

• Preoperative assessment as usual especially for the cardiovascular system.

• General anesthesia or regional anesthesia (combination of spinal and epidural is ideal) according to the patient's condition and the length of surgery.

• Besides the standard monitors, invasive monitors are recommended such as invasive blood pressure and central venous pressure.

b- Chronic Peripheral Arterial Occlusive Disease (Atherosclerosis)

Atherosclerosis is the most important cause affecting the distal abdominal aorta, coronary, cerebral, iliac, femoral, or subclavian vessels. The patients are usually on aspirin, dipyridamole, or antiplatelet therapy.

1- Distal Abdominal Aorta or Iliac Arteries (Bypass of Aorto-Iliac Occlusion):

The same anesthetic considerations as in abdominal aortic surgery except that the clamp of the aorta is only a side clamp allowing some peripheral blood flow; therefore, less hypotension and metabolic changes occur.

2- Femoral Arteries.

3- Subclavian Steal Syndrome.

Occlusion of the subclavian or innominate artery proximal to the origin of the vertebral artery by atherosclerosis causes reversal of flow through the ipsilateral vertebral artery into the distal subclavian artery. This diverts the blood away from the brain to supply the arm (subclavian steal syndrome) causing central nervous symptoms as syncope, vertigo, ataxia, hemiplegia; which is increased by exercise of the ipsilateral arm (with a decrease in the pulse or blood pressure in this arm) (figure 24-14).

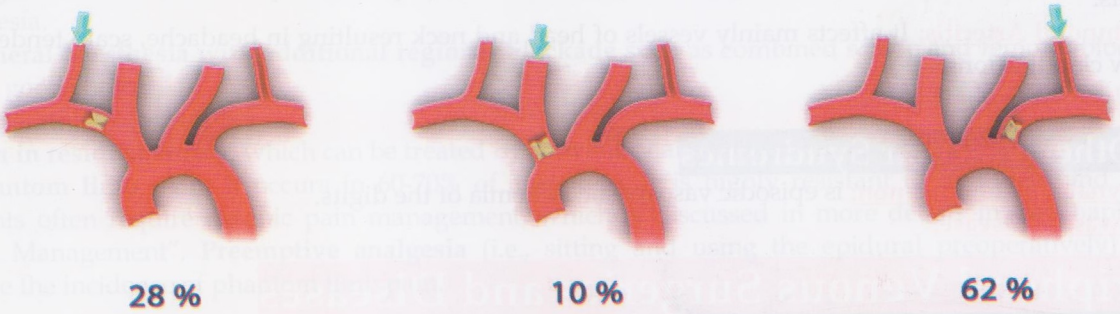


Figure 20-14: Subclavian steal syndrome

4- Coronary-Subclavian Steal Syndrome.

It occurs as a complication of using internal mammary artery for coronary revascularization with proximal incomplete stenosis in the left subclavian artery. It causes reversal of the blood flow via the patent internal mammary artery graft. This results in myocardial ischemia, central nervous ischemia, and decreased arterial blood pressure in the ipsilateral arm (figure 24-15).

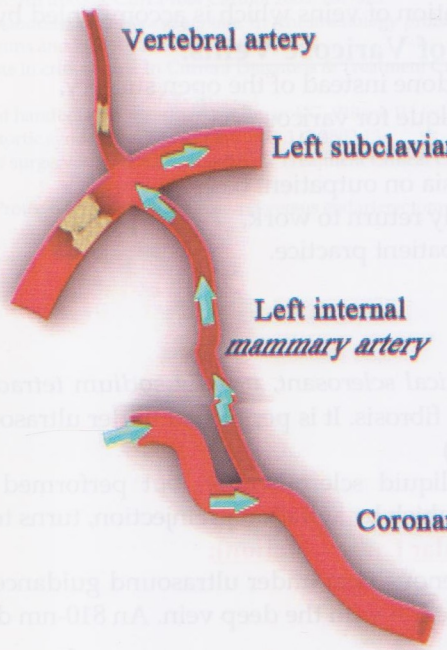


Figure 20-15: Coronary subclavian steal syndrome

Treatment:

1- Treatment of peripheral arteries: by **angioplasty with a balloon catheter or bypass surgery** e.g., femoro-femoral bypass or femoro-popliteal bypass. The same anesthetic management as that of abdominal aortic surgery is applied in addition to heparin administration (i.v. or local).

2- Subclavian steal syndrome: It is treated by subclavian endarterectomy.

3- Coronary subclavian steal syndrome: It is treated by coronary revascularization and the patient is managed as if with severe ischemic heart disease.

c- Systemic Vasculitis

It may affect cerebral, coronary, or renal arteries resulting in strokes, ischemia, or renal failure respectively. Systemic vasculitis includes:

1- Takayasu's arteritis: It is a rare syndrome characterized by progressive vasculitis of systemic and pulmonary vessels especially in young Asian.

2- Thromboangitis obliterans (Buerger's disease): It affects vessels of extremities especially men. The most important cause is tobacco use. It is due to autoimmune disease against the nicotine.

3- Wegner's granulomatosis: It is characterized by formation of necrotizing granulomas in systemic vessels.

4- Temporal Arteritis: It affects mainly vessels of head and neck resulting in headache, scalp tenderness, or jaw claudications.

5- Polyarteritis Nodosa.

d- Other Vascular Syndromes

1- Raynaud's phenomenon: is episodic vasospastic ischemia of the digits.

2- Kawasaki disease.

Peripheral Venous Surgeries and Diseases

1- Deep Venous Thrombosis

It is discussed in the chapter of "Respiratory Diseases".

2- Varicose Venous Disease

The procedure involves removal of tortuous veins of the lower extremities with/without high tie and strip of long saphenous vein. **Patients** are usually **young and fit**. **Blood loss** may be reduced by **elevating the legs**.

General or regional anesthesia is used according to patient's medical condition and presence of contraindications. In stripping of long saphenous vein, some surgeons prefer general anesthesia to regional anesthesia to avoid vasodilatation of veins which is accompanied by increased hemorrhage.

Recent Advances in Treatment of Varicose Veins:

Minimal invasive techniques are now done instead of the open surgery.

Advantages of minimal invasive technique for varicose veins:

- It is associated with lower complications.
- It can be done under local anesthesia on outpatient basis.
- It allows early ambulation and early return to work.
- It is less expensive if based on outpatient practice.

They include:

1- Injection Sclerotherapy: It is either:

a- Liquid Sclerotherapy:

It involves direct injection of a chemical sclerosant, usually sodium tetradecyl sulphate (STD), into the vein, initiating thrombo-phlebitis and fibrosis. It is performed under ultrasound guidance.

b- Foam Sclerotherapy: (better results)

It employs the same principles of liquid sclerotherapy, but performed using a smaller quantity of sclerosant such as polidocanol 0.5%, which by agitation preinjection, turns to foam.

2- Endoluminal Ablation (Endovascular Laser Ablation):

- It involves cannulation of the saphenous vein under ultrasound guidance and a Seldinger technique to pass a narrow gauge sheath to the junction with the deep vein. An 810-nm diode laser fiber is positioned 2 cm from the junction.

• Perivenous infiltration of 0.1% lignocaine is then performed under ultrasound guidance, around the full length of the vein. This provides good analgesia, compresses the vein onto the laser ensuring good opposition, and acts as a method to prevent thermal damage to surrounding tissues, particularly nerves.
• The laser is fired as it is gradually withdrawn from the vein and on completion; a compression bandage or stocking is applied.

Amputations

They are either below knee, through knee, above knee, Symes, digits…etc.

Anesthesia Problems and Considerations:

Patients are often very sick, bed-ridden, or diabetic with significant cardiovascular disease, which should be assessed preoperatively. Some patients are septic due to the presence of the necrotic dead tissues, which should be amputated, thus operation should not be cancelled for this reason.

Choice of Anesthesia:

It should be individualized according to the patient's condition and presence of contraindications.

• **Regional anesthesia** as spinal or epidural with sedation is a good choice and allows pre-emptive analgesia.
• **General anesthesia with additional regional blockade** such as combined sciatic and femoral blocks is also a good choice.

Postoperative pain: is either

• **Pain in residual stump**, which can be treated by conventional analgesic techniques.
• **Phantom limb pain**: It occurs in 60-70% of amputees. It is highly resistant to treatment and these patients often require chronic pain management, which is discussed in more details in the chapter of "Pain Management". **Preemptive analgesia** (i.e., sitting and using the epidural preoperatively) may reduce the incidence of phantom limb pain.

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CARDIAC SURGERY

25

• Coronary artery disease (CAD) • Percutaneous transluminal coronary angioplasty (PTCA) • Coronary artery bypass grafting (CABG) • Cardiopulmonary bypass (CPB) or extra-corporeal circulation (ECC) Components Patho-physiological effects • Myocardial preservation or protection Intentional (induced) hypothermia Potassium cardioplegia • Anesthetic management of cardiac surgery Preoperative management Intraoperative management Postoperative management	• Redo coronary arterial bypass graft • Emergency coronary arterial bypass graft (failed angioplasty) • Anesthetic management of cardiac surgery in pediatric patients • New aspects for myocardial revascularization. • Extracorporeal membrane oxygenation (ECMO). • Cardiac transplantation • Anesthesia for a patient with a transplanted heart • Pericardial diseases Acute pericarditis Chronic constrictive pericarditis Pericardial effusion Cardiac tamponade

Coronary Artery Disease (CAD)

Patients with ischemic heart diseases can present with:

1- Chronic stable angina (angina pectoris).

2- Acute coronary syndrome (with ischemic type chest pain): It includes one of the following clinical conditions:

a- ST-segment elevation myocardial infarction (with positive troponin/creatine kinase myocardial bound "CK-MB").

b- Non-ST- segment elevation (non-Q wave) myocardial infarction (with positive troponin/CK-MB).

c- Unstable angina; if troponin/CK-MB is negative.

Pathophysiology, causes, risk factors, clinical presentations, investigations, and treatment of coronary artery disease are discussed in more details in chapter "Cardiovascular Disease".

Triple vessel coronary artery disease usually involves the following vessels:

- The right coronary artery.
- The left anterior descending branch.
- The left circumflex branch.

Coronary angiography and cardiac catheterization is done first to assess the patient's benefit before:

- Percutaneous trans-luminal coronary angioplasty or
- Coronary artery bypass grafting surgery (CABG).

Percutaneous Transluminal Coronary Angioplasty (PTCA)

It was introduced in 1977 by a Swiss physician named Andreas Gruntzig.

Technique:

It involves the passage of a small (3F) catheter into the involved coronary artery and through the stenosis **with the balloon** portion of the catheter straddling the stenosis; inflations are performed that cause **widening of the stenotic lumen**. The luminal widening is achieved by a controlled injury involving, to a varying degree, plaque compression, intimal fissures, and medial stretching.

Sometimes it is needed to apply a coronary stent either bare stent (without a drug) or drug-eluting stent.

Indications:

It is therapeutic in patients with disabling ischemic symptoms despite good medical therapy and **focal obstructive coronary disease** regardless of the cause for example:

1- Isolated discrete **proximal** single vessel disease.

2- **Proximal double** vessel disease.
3- **Post-coronary artery bypass grafting with new stenotic lesions** or stenosis at the distal anastomosis.
4- **Re-stenosis after PTCA**.
5- **Contraindications to** coronary artery bypass grafting **(CABG).**
6- Coronary stenosis **after cardiac transplantation**.
7- Occluded vessels of **< 6 months in duration and < 15 mm in length**.
8- **Postoperative therapy** for revascularization.

Contraindications:

1- **Left main CAD** in which the distal vessels are not protected by at least one completely patent bypass graft.
2- **Multi-vessel** disease with **severe diffuse atherosclerosis**.
3- **Absence of significant obstructing lesions.**
4- Absence of **a formal cardiac surgical program within the institution**.

Results:

The **primary success rate** is about **90%. Re-stenosis** occurs in **30% of patients 6 months after** the procedure. Dilatation is again performed with a 90% success rate.

Complications of Cardiac Catheterization

a- Vascular Access Complications:

- Dissection.
- Occlusion of vascular site.
- Thrombosis.
- Large hematomas.

b- Central Nervous Complications:

- Strokes due to embolization of intracardiac thrombi, aortic intimal plaque disruption, catheter thrombosis and embolization, dissection of carotid arteries or air injected inadvertently during catheterization.

c- Other Complications:

- Cardiovascular complications such a myocardial infarction, arrhythmias, cardiac tamponade, and aortic dissection.
- Radiological contrast medium-related problems that include histamine-mediated reactions (e.g., urticaria, angioedema, and hypotension) and volume depletion and hypotension secondary to the osmotic diuresis and acute renal failure.

Coronary Artery Bypass Grafting (CABG)

Indications:

Generally, the patients who are not suitable for PTCA are usually referred for CABG. Therefore, the patients for CABG are usually older patients with more diffuse CAD and decreased left ventricular function, for example:

1- **Unstable angina** or episodes of prolonged myocardial ischemia.
2- **Unacceptable angina**, despite optimal medical therapy.
3- **Repeated angina** after myocardial infarction.
4- **Prinzmetal's angina (variant angina)** with coronary artery obstruction.
5- **High grade left main coronary artery obstruction, triple- or double vessel obstruction.**
6- **Proximal left anterior descending artery obstruction.**
7- **Acute myocardial infarction, cardiogenic shock, or intractable ventricular arrhythmias**.
8- Stable angina pectoris **that interferes with the desired life style**.

Results:

Perioperative myocardial infarction rate is 4-6%. The overall operative mortality rate of CABG at major medical centers is about 1%, but for a redo, it is 2-3% (4-5% with valve surgery). The 10-year survival rate among the group receiving the internal mammary artery graft as compared with the group receiving saphenous vein grafts is 93.4% versus 88% for those with one vessel disease. At the end of the 1st 10 postoperative years, the patency of internal mammary artery grafts is 85-95% while the patency of saphenous vein grafts is only 38%-45%.

Cardiopulmonary Bypass (CPB) Extra-Corporeal Circulation (ECC)

• It is a technique that diverts venous blood away from the heart, adds O_2, removes CO_2, and returns the blood to a large artery. As a result, all blood flowing through the heart and most of that through the lungs ceases when CPB is fully established. The extracorporeal circuit is in series with the systemic circulation and provides both artificial ventilation and perfusion.

Total CPB begins with drainage of systemic venous blood in a reservoir via a venous cannula. A separate pump-driven cardiotomy suction device can be added to return shed blood from the operative field to the same reservoir. Blood then is actively pumped through an oxygenator/heat exchanger and back to the systemic circulation via the arterial cannula. A number of additional specialized circuits deliver cardioplegia, provide pulmonary venous and collateral drainage (vents), or perfuse localized areas. Arterial and venous cannulas are usually placed in the ascending aorta and right atrium, but a number of locations are used on an individual basis.

• Operation of the CPB machine requires a perfusionist (a highly specialized technician).

• Optimal results with CPB can be obtained only by close cooperation and communication between the surgeon, anesthesiologist, and perfusionist.

Components of the Cardiopulmonary Bypass Circuit

The bypass machine consists of an integrated, disposable unit made up of reservoir, oxygenator, and heat exchanger connected via a series of centrifugal or roller pumps on the permanent part of the machine (figure 25-1 and 25-2).



Figure 25-1: A Heart-lung machine

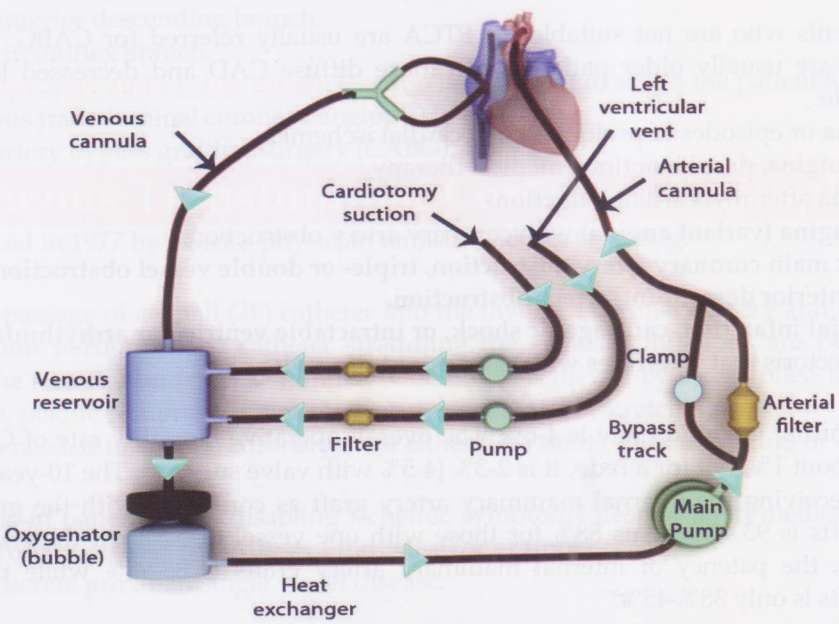


Figure 25-2: Components of CPB

The Primary Fluid (and Hemodilution)

Volume:

Before the use of CPB, it must be primed with fluid devoid of any bubbles. The volume varies with the size of the oxygenator used and the tubing volume. It is usually **1500-2000 mL**.

Type of Priming Fluid:

a- A balanced salt solution (or compound Na lactated solution) is generally used. Other additional compounds are frequently added such as:

1- **Colloid** (albumin or hetastarch).
2- **Mannitol** (for renal protection) 200 mL 20%.
3- **Heparin** (to cover the thrombogenic surface of the CPB circuit); 500-1000 units.
4- **Bicarbonate.**
5- **Potassium** (if cardioplegia will not be used).
6- **Antibiotics.**

b- Blood: It is used in the following conditions:

- **Small pediatric patients**.
- **Severely anemic adult patients** (i.e., with **hematocrit < 30%**) to avoid severe hemodilution because priming fluid causes hemodilution, which decreases the hematocrit up to 25% in most patients.

Effect of Priming Fluid:

It produces hemodilution, which has advantages and disadvantages:

Advantages of Hemodilution:

- It increases the microcirculation due to decreased blood viscosity.
- It decreases the metabolic acidosis.
- It increases the urine output.
- It decreases the blood demands.
- It decreases the incidence of hepatitis, acquired immune deficiency syndrome (AIDS) or reactions from blood transfusions.

Disadvantages of Hemodilution:

- It decreases the O_2 carrying capacity.
- It causes postoperative extracellular fluid overload.
- It increases the risk of pulmonary edema.
- It causes hypotension from the decreased viscosity and peripheral resistance.
- It decreases the concentration of Ca^{++}, Mg^{++}, phosphate, and zinc.

I) Venous Reservoir

It receives blood from the patient (usually from the right atrium or from both inferior and superior vena cavae) via one or two venous cannulas **by the effect of gravity**.

Factors Affecting Blood Flow to the Reservoir:

1- Blood flow is directly proportional to the difference in **the height between the patient and the reservoir (i.e., the gravity).** Blood flow can be improved by raising the level of the operating table.
2- Blood flow is inversely proportional to **the resistance of the cannulas and tubing systems.**
3- Priming the machine creates **a siphon effect.**
4- Venous pressure is normally low; it has a very little effect.

Precautions:

1- Entrainment of air can produce an air lock that may prevent blood flow.
2- **The fluid level in the reservoir is critical**. If the reservoir empties, air can enter the main pump and causes **fatal air embolism**; therefore, a low reservoir level alarm is typically present.

II) Oxygenator

Blood is drained by gravity from the bottom of the venous reservoir into the oxygenator.

Function:

1- The blood equilibrates with the gas mixture (primarily O_2).
2- CO_2 and volatile anesthetics are also frequently added at the oxygenator gas inlet.

Types of Oxygenators:

a- Direct gas interface such as:

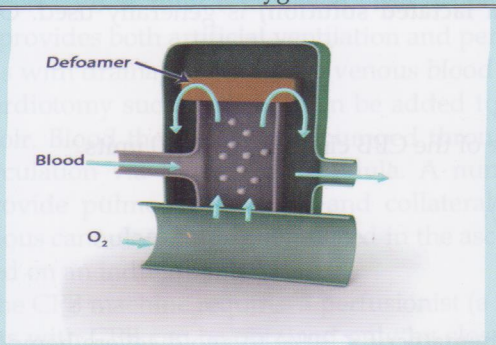
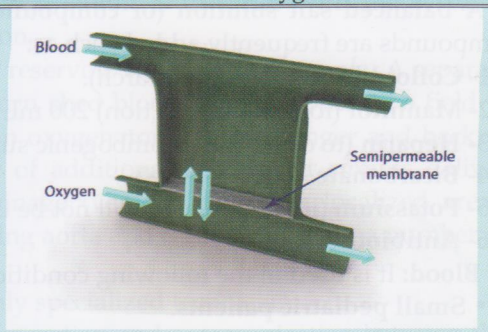
- Disc type
- Vertical screen type.

Both are not used now because they are not disposable and difficult to clean and re-sterilize.

- Bubble type: disposable and of low cost.

b- Without a gas interface:

- Membrane type: is the most commonly used (figure 25-3).
- Fluid type: using fluorocarbon liquid (figure 25-4).

	Bubble Oxygenator	Membrane Oxygenator
	  Figure 25-3	  Figure 25-4
Idea	• Tiny bubbles (foam) are formed where the O_2 passes through **small holes** at the base of a blood column. Bubbles are then removed by passing blood past **a de-foaming agent** such as a charged silicon polymer. Oxygenation depends on: • **The surface area** (bubble size and number). The smaller the bubbles, the larger the surface area for blood to equilibrate with the inflowing gases. • **Transit time** of the blood in the oxygenation column. CO_2 elimination: is **directly proportional to O_2 flow.**	• The blood-gas interface is very thin containing a **gas-permeable silicon membrane** through which O_2 diffuses. Oxygenation is inversely related to the **thickness of the blood film** in contact with the membrane. CO_2 elimination: is **directly proportional to O_2 flow.**
Advantages	• Less expensive.	• **Less traumatic** to formed elements in the blood. It is preferred if a long bypass period is anticipated. • No risk of air embolism.
Disadvantages	1- **More traumatic** to formed elements in blood (red blood cells and platelets). This becomes more significant with longer period of bypass (> 4-6 hours), actually before 2 hours no difference is noticed between the 2 types. 2- Increased risk of **air embolism.** 3- **Protein denaturation.** 4- **Large priming fluid** is needed.	• **More expensive.**

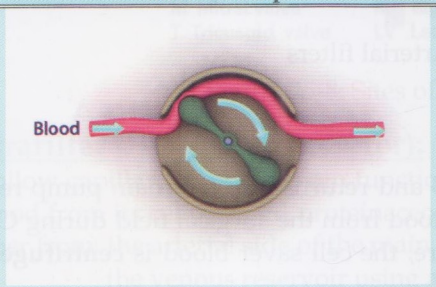
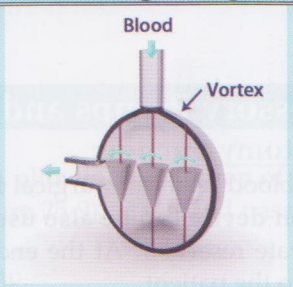
III) Heat Exchanger

The blood from the oxygenator enters the heat exchanger.

Function: It either **cools or warms the blood** depending on the temperature of the water flowing through the exchanger **(4 - 42°C)** as heat transfer occurs by **conduction.** Cold or hot water entering the unit at one end with blood entering at the other provides an efficient countercurrent flow system.
Precautions: Because gas solubility decreases as blood temperature increases, **a filter** is built into the unit to catch any bubbles that may form during re-warming.

IV) Main Pump

Types:
1- A double headed non-occlusive roller pump (figure 25-5).
2- A centrifugal pump (more preferable) (figure 25-6).
N.B: The pump is normally placed after a bubble oxygenator but must be placed before a membrane oxygenator because the latter type offers greater resistance to blood flow than the bubble type.
3- A ventricular type pneumatic or hydraulic pump: is pulsatile and more powerful but cumbersome; therefore, it is not used nowadays.

	Roller Pump	Centrifugal Pump
	 Figure 25-5	 Figure: 25-6
Idea	It produces flow by compressing a large bore tube in the main pumping chamber as the heads turn.	It consists of **a series of cones (3 in number) in a plastic housing (vortex).** As the cones spin at 3000- to 4000 rpm, the centrifugal forces created propel the blood from the centrally located inlet to the periphery.
Characters	1- **Blood flow is directly proportional to the number of revolutions/minute.** The **speed** of the rollers is **constant** to pump blood regardless of the resistance e.g., kinking or clamping of the arterial line; therefore, there is **an increased risk of rupture of connections**. Some centers use **pressure gauge** on the arterial inflow line to avoid this type of a disaster. 2- There is **subtotal occlusion** of the tubing to **prevent excessive trauma** to the blood elements. 3- It produces **continuous non-pulsatile flow**. Pulsatile flow can be produced in modified types (see later). 4- **Inflow in-responsiveness**. 5- A greater **risk of micro-air emboli**.	1- **Blood flow is pressure sensitive** and afterload dependent. Blood flow must be **monitored by an electro-magnetic flowmeter**, as an increase in the distal pressure decreases the flow and must be compensated by an increase in the pump speed. There is **less risk of increased arterial line pressure and so disconnection.** 2- There is **no occlusion** to the tubing; therefore, it is **less traumatic** to the blood elements. 3- It produces **continuous non-pulsatile flow**. Pulsatile flow is not possible. 4- **Inflow responsiveness** i.e., if a large quantity of air is introduced into the pump, cohesive forces will no longer exist between layers of blood and thus pumping will stop. 5- A **less risk** of micro-air emboli because small low density air bubbles are trapped in the center of the vortex (as air bubbles are less dense).

The Pulsatile Pump:

Value: It offers more physiological conditions, but the value of this is controversial.
- It improves tissue perfusion.
- It improves O_2 extraction.
- It decreases the release of stress hormones.
- It decreases systemic vascular resistance during CPB.

Therefore, it increases renal and cerebral blood flow.
Types: The pulsatile flow can be produced by one of the following methods:
- **The modified roller pump**: by instantaneous variations in the rate of rotation of the roller heads.
- **The ventricular type pump**.
- An indwelling **intra-aortic balloon pump**.

V) Arterial Filter

A final in-line **arterial filter (27- 40 µm)** is used before the blood reaches the patient via a cannula usually in the ascending aorta (figure 25-7).

Value:

- **It prevents systemic embolism** by particulate matters e.g., thrombi, fat globules, Ca^{++}, or tissue debris.
- **It traps air,** which can be bled out through a built-in stopcock.

Precautions:

There is **a bypass limb** (normally clamped), which will open if the filter is clogged or develops high pressure (measured before the filter).



Figure 25-7: Arterial filters

VI) Accessory Pumps and Devices

A- Cardiotomy Suction:

It aspirates blood from the surgical field during CPB and returns it to the main pump reservoir. **A cell-saver suction device can be also used.** It aspirates blood from the surgical field during CPB and returns it to a separate reservoir. At the end of the procedure, the cell saver blood is **centrifuged, washed** and given back to the patient.

Disadvantages:

- The excessive use of cell saver suction (instead of cardiotomy suction) during CPB depletes CPB circuit volume.
- Excessive suction negative pressure leads to excessive red cell trauma and precludes blood salvage from that source.
- The cardiotomy suction may be a major cause of hemolysis and emboli during CPB.

B- Cardioplegia Pump:

Cardioplegia is administered by either:

- **An accessory pump**, which allows optimum control over the infusion pressure, rate, and temperature (by a separate heat exchanger) or
- A cold i.v. fluid bag, which is **squeezed under pressure.**

C- Left Ventricular Vent:

- With time, **even after institution of total CPB, 2-5% of blood re-accumulates in the left ventricle** due to:
  - Residual pulmonary flow from, **physiological shunts** i.e., from bronchial arteries (which arise directly from the aorta or the intercostals arteries), thebesian vessels (which drain blood directly from the heart to its cavity), or pleural vessels. They end in the left atrium without passing via the lung.
  - **Aortic regurgitation**, which results from structural valvular abnormalities or surgical manipulation of the heart resulting in functional aortic regurgitation.
  - **Extra-cardiac left to right shunts** e.g., patent ductus arteriosus, Blalock-taussig, Waterston, and Potts shunts.
- Left ventricular distention **compromises myocardial preservation** and causes **post-pump heart failure;** therefore, requiring decompression (venting).
- Left ventricular vent can be produced by a catheter inserted into left ventricle at one of the following sites (figure 25-8):
  - The junction of the right superior pulmonary vein and left atrium then, via the left atrium and mitral valve into the left ventricle (the most common).
  - The left ventricular apex.
  - The aortic root by a cardioplegia cannula.
  - The pulmonary artery or left atrium only.

  The blood, which is aspirated by the vent pump, passes through a filter and is returned to the venous reservoir.

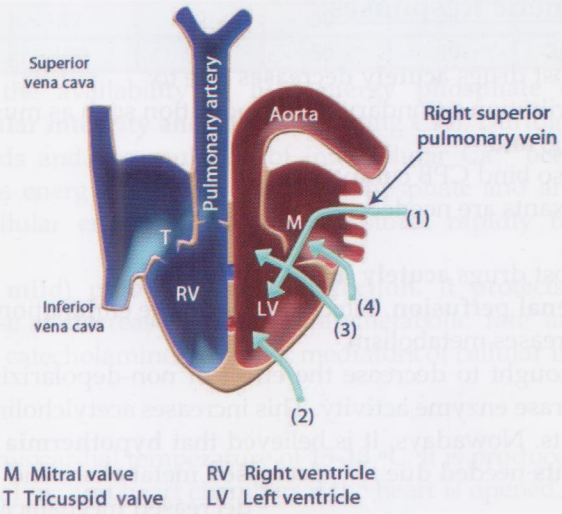


Figure 25-8: Sites of left ventricular vent

D- Hemo-ultrafilter (Hemo-concentrator):

It consists of hollow capillary fibers that can function as membranes, allowing separation of the aqueous phase of the blood from its cellular and proteinaceous elements (figure 25-9). The blood passing through the fibers is either from: the arterial side of the main pump or
the venous reservoir using an accessory pump.

As hydrostatic pressure forces water and electrolytes across the fiber membrane, effluents of up to 40 mL/min can be removed.

Value: To increase the patient's hematocrit without transfusion.



Figure 25-9: Hemo-concentrators

Patho-physiological Effects of CPB

A) Hormonal Responses:

Initiation of CPB causes a marked increase in stress hormones such as catecholamines, cortisol, arginine-vasopressin, and angiotensin due to the stress and the decreased metabolism secondary to:

- hypothermia and
- exclusion of the pulmonary circulation where many of these substances are normally broken down.

B) Humoral Responses:

CPB induces **coagulation/inflammation interaction**. It is sometimes called **coagflammation**. CPB induces coagulation and inflammation responses initiating a cascade of procoagulant and pro-inflammatory events. The mediators of coagflammation during CPB include thrombin, cytokines, proteases, free radicals, arachidonic acid metabolites, platelet-activating factor, nitric oxide synthesis/inhibition, endothelin, endotoxins, tissue factors, complement, adhesion molecules, extravascular leukocytes migration, kallikrein/bradykinin system, and selectins. These mediators vary from organ to organ and patient to patient. This is due to:

- Contact of blood with the internal surfaces of the CPB system.
- Mechanical trauma.
- A systemic inflammatory response syndrome (SIRS) (similar to that of sepsis and trauma), which can occur. If it is severe and prolonged, it produces: ▫ Generalized edema.
  ▫ Adult respiratory distress syndrome.
  ▫ Acute renal failure.

C) Altered Pharmacokinetic Responses:

1- At the onset of CPB:

- Serum concentration of most drugs **acutely decreases** due to:
  - increased volume of distribution secondary to hemodilution such as muscle relaxants.
  - decreased protein binding, and
  - some drugs as opioids also bind CPB components.

Therefore, more muscle relaxants are needed.

2- During the course of CPB:

- Serum concentration of most drugs **acutely increases** due to:
  - **decreased hepatic and renal perfusion**, which decreases the elimination of drugs and
  - **hypothermia,** which decreases metabolism.
- Hypothermia has been thought to decrease the effect of non-depolarizing muscle relaxants because there is decreased cholinesterase enzyme activity. This increases acetylcholine, which competes with non-depolarizing muscle relaxants. Nowadays, it is believed that **hypothermia decreases the doses of non-depolarizing muscle relaxants** needed due to: ▫ decreased metabolism and
  ▫ decreased mechanical contractility of muscles.
- Drugs may **redistribute** from the peripheral to the central compartments.
- **Heparin** increases release and activation of **lipoprotein lipase**, which hydrolyzes the plasma triglycerides into free fatty acids. This causes **competitive inhibition of the drugs binding to plasma proteins**.

3- After CPB and postoperatively:

- Serum concentration of drugs is also **altered** due to alterations in α_1-acid glycoprotein, which changes drug binding.

Myocardial Preservation or Protection

- The aim of myocardial preservation is to decrease the myocardial damage induced by the period of ischemia associated with cardiopulmonary bypass.
- Understanding of the **patho-physiology of the ischemic heart diseases** allows proper myocardial preservation and protection. **Preoperative, intraoperative, and postoperative managements of ischemic heart disease** aim to protect the heart perioperatively such as reassurance of the patient during preoperative visit, proper preoperative assessment, avoiding the pressor response of intubation, and close postoperative monitoring. The patho-physiology of myocardial ischemia and the perioperative managements are discussed in chapter "Cardiovascular Diseases".
- Additional factors increasing risk of myocardial ischemia, which should be avoided, include:
  - **Imbalance between myocardial O_2 demand and supply** (the main factor).
  - **Reperfusion injury** following a period of ischemia especially in patients in the New York Heart Association (NYHA) functional class IV and in those who have ventricular hypertrophy or severe coronary artery disease.
  - **Prolonged aortic cross clamping during CPB > 120 min**.
  - **Excessive surgical manipulation** or distortion of the coronary vessels.
  - **Ventricular fibrillation**, which can double myocardial O_2 consumption.
  - **Ventricular distention**, which increases myocardial O_2 consumption and reduces O_2 supply by interfering with subendocardial blood flow.
  - The use of **inotropes** and excessive administration of Ca^{++}.
  - **Air embolism**; therefore de-airing of cardiac chambers in open-heart procedures, before and during initial cardiac ejection, is important in preventing coronary embolism (and cerebral strokes). De-airing of grafts during coronary bypass procedure is similarly important.
- The most important procedures performed during CPB to preserve the heart are intentional hypothermia and administration of cardioplegia.

Intentional (Induced or Therapeutic) Hypothermia

Effects of Hypothermia:

- Hypothermia abolishes the energy expenditure associated with both electrical and mechanical activity and decreases cellular energy requirements to the minimal. It **decreases the basal metabolic O_2 consumption** as metabolic O_2 consumption is generally **halved with each 7-8 °C decrease in body temperature**.

Temperature	°C	37	32	30	28	25	20	10
O_2 Consumption	%	100	60	50	40	25-30	20	10

• Hypothermia **preserves** the availability of **high-energy phosphate compounds** thus, allowing **maintenance of normal cellular integrity and function** during CPB. During ischemia, depletion of high-energy phosphate compounds and accumulation of intracellular Ca^{++} occur (Ca^{++} acts on contractile proteins that further depletes energy supplies). Creatine phosphate and anaerobic metabolism become the principal sources of cellular energy. These energy stores rapidly become depleted leading to progressive acidosis.

• **Hypothermia** (especially **mild**) produces **neuro-protection.** It protects against transient (but not permanent) ischemia because it decreases the cerebral metabolic rate and decreases the release of excitatory neurotransmitters, catecholamines, or other mediators of cellular injury.

Types and Values:

a- Topical Hypothermia:

It is applied to reach a local myocardial temperature of **15-18 °C**. It is produced by:

- **Ice slush** in the pericardial sac and heart chambers if the heart is opened.
- **Cold cardioplegia.**

b- Systemic Hypothermia:

It is produced by heat exchangers in the oxygenator. The degrees of systemic hypothermia include:

a- Tepid hypothermia (32-35 °C): It has recently been used (see later).
b- Mild hypothermia (26-32 °C): It is the most common one used.
c- Moderate hypothermia (20-25 °C).
d- Deep profound hypothermia (15-19 °C).

Deep Profound Hypothermia: 15-19 °C.

• It allows total circulatory arrest up to 60 minutes. It is used for complex surgical repair; as during circulatory arrest, both the heart and CPB machine are stopped. This allows the surgeon to remove the cannulas, which may have distorted the anatomy, and allows more precise repair of the lesion under optimal conditions i.e., **a bloodless and cannula-free field.**

• **Q_{10}:**

▫ Q_{10} defines the **ratio of organ O_2 consumption at a defined temperature to the O_2 consumption at a temperature 10°C (18°F) lower.** Q_{10} is **the temperature coefficient** that describes the reduction in cerebral metabolism for every 10°C decrease in temperature.

▫ The **cerebral Q_{10}** is approximately **3.65 in children and 2.3 in adults** i.e., between 27 °C and 37 °C, the Q_{10} for a child is 3.65 and for an adult is 2.3. This means; for every 10 °C increase in temperature e.g., from 27 °C to 37 °C, the cerebral metabolic rate nearly doubles. Conversely, for every 10 °C decrease in temperature e.g., from 37 °C to 27 °C, the cerebral metabolic rate decreases about 50% and also the cerebral metabolic rate decreases another 50% if the brain temperature decreases from 27 °C to 17 °C.

• In general, cerebral metabolism decreases with hypothermia in an exponential manner;

Cerebral metabolic rate of O_2 ($CMRO_2$) decreases by 50% at 27 °C.
60% at 25 °C.
75% at 20 °C.
85% at 10 °C.

• Based on the assumption that 3-5 minutes of normothermic arrest does not produce ischemic brain damage, the Q_{10} data predict that a safe arrest time at 15 °C would be **50-90 minutes, but clinical evidence suggests** that the duration of a safe circulatory arrest period is **50-60 minutes in neonates, infants, and children. Infants tolerate** hypothermic circulatory arrest **better** than older children and adults.

• Estimated safe periods of the circulatory arrest at different body temperatures:

Nasopharyngeal Temperature	37°C	32	30	25	20	15
Estimated Safe Time	3-5 min	5-9	9-12	14-24	28-46	53-89

• The lower the temperature,
the longer the time needed for cooling and re-warming,
the lower the CPB flow e.g., at 20°C temperature, a flow of 1.2 L/min/m^2 is adequate,
the higher the risk of arrhythmias e.g., at temperatures < 28-29°C, ventricular fibrillation can occur; therefore, cardioplegia should start immediately because ventricular fibrillation rapidly consumes high energy phosphates, which jeopardizes myocardial preservation.

Potassium Cardioplegia

Action (Value):

"Cardio-" means heart and "plegia" means to paralyze.

- It is **a chemical solution for arresting the myocardial electrical activity**.
- After initiation of CPB, induction of hypothermia, and aortic cross clamping, the coronary circulation is perfused with cold cardioplegia resulting in increased extracellular K^+ concentration. This increases K^+ shift intracellularly, so the trans-membrane potential is decreased (less negative inside). This interferes with the normal Na^+ influx (and K^+ efflux) during the initial phase of myocardial depolarization decreasing the rate of rise, amplitude, and conduction velocity of subsequent action potentials. Eventually Na^+ channels are completely inactivated, action potentials are abolished, and the heart is arrested in diastole.

Components of K^+ Cardioplegia:

Although the exact composition varies from center to center, the essential elements of cardioplegia are the same.

Typical Components	Function and Comments
• $K^+ < 50$ (usually 20-40) mEq/L	• The function of K^+ is as above. • **Avoid higher levels** because they can be associated with a paradoxic increase in myocardial energy requirements and increase the K^+ loads.
• Na^+ 100-120 mEq/L.	• It is less than that of plasma because ischemia tends to increase the intracellular Na^+ content.
• Chloride 110-120 mEq/L.	• It maintains electro-neutrality.
• Ca^{++} 0.7 mEq/L.	• It acts as a membrane-stabilizing agent. It stabilizes lysosomes and the cell membrane, maintaining cellular integrity.
• Mg^{++} 15 mEq/L.	• It controls excessive Ca^{++} influx intracellularly; so, relaxes the heart.
• Glucose 28 mmol/L (glutamate, or aspartate) + insulin	• It acts as an energy substrate and improves intracellular shift of K^+.
• Bicarbonate 27 mmol/L (histidine and tromethamine 'THAM' are alternative buffers).	• It acts as a buffer to increase the pH between 7.4-7.8, preventing excessive build up of acid metabolites due to ischemia, and increasing intracellular shift of K^+ because alkalotic perfusates are reported to produce better myocardial preservation.

Additional Components	Function
• Hypertonic agent e.g., Mannitol	• To control cellular edema
• Free radical scavenger e.g., Mannitol	• To get rid of free radicals
• Glucocorticoids	• To act as a membrane stabilizing agent
• Procaine	• To act as a membrane stabilizing agent
• Ca^{++} channel blockers	• To decrease the metabolic demand
• β blockers	• To decrease the metabolic demand
• Prostacyclin	• To produce an anti-platelet effect
• Nitroglycerin	• To dilate coronary vessels

Vehicle of Cardioplegia:

Cardioplegia is administered as:

a- Crystalloid cardioplegia: The components of cardioplegia are added to a crystalloid solution.

b- Blood cardioplegia: It is used in **high-risk patients**, where the components of cardioplegia are added to the blood. Advantages of blood cardioplegia: (controversial)

- It **provides more O_2 to tissues** as enough O_2 is dissolved in the plasma to sustain metabolism with little O_2 released from hemoglobin during hypothermia.
- It provides a **more buffering capacity** due to presence of the histidine buffering system in red blood cells.
- It **decreases myocardial edema** due to the oncotic pressure of the blood.
- The risk of **Ca^{++} paradox** after ischemia **is decreased** and functional recovery is improved due to the physiological Ca^{++} concentration provided by the blood.
- The presence of **the enzyme catalase of red blood cells** may scavenge free radicals produced by ischemia.
- **Capillary perfusion is improved** and becomes more homogenous due to the presence of red blood cells.

• Results of **clinical studies** show that blood cardioplegia **improves contractility** late in the post-operative course when compared with crystalloid cardioplegia.

Preparation of Cardioplegia:

a- Crystalloid cardioplegia is prepared as follows: 20 mEq KCl + 10 mEq $NaHCO_3$ are added to 1000 mL of 5% glucose in 0.225% salt solution. Its final pH is 7.83, K^+ is 20 mEq/L and it has an osmolarity of 380 mOsm/L.

b- Blood cardioplegia is prepared as follows: 4 parts of bypass blood are mixed with one part of the cardioplegic solution.

Method of Administration of Cardioplegia:

Cardioplegic solution should be **rapidly infused under pressure (about 300 mmHg)** by one (or more) of the following methods:

1- A small catheter inserted **proximal to the cross clamping of the aorta.**

2- Directly into the **coronary ostia,** if the aorta is opened.

3- Through the **aorto-coronary graft,** if the surgeon elects to do the distal anastomosis first.

4- **Continuous retrograde infusion** in severe coronary obstruction via a catheter inserted in the **coronary sinus** and threaded into the coronary vein, because cardioplegia, if given by antegrade infusion, it may not reach areas distal to high-grade coronary obstructions (the areas that need it most) (figure 25-10).

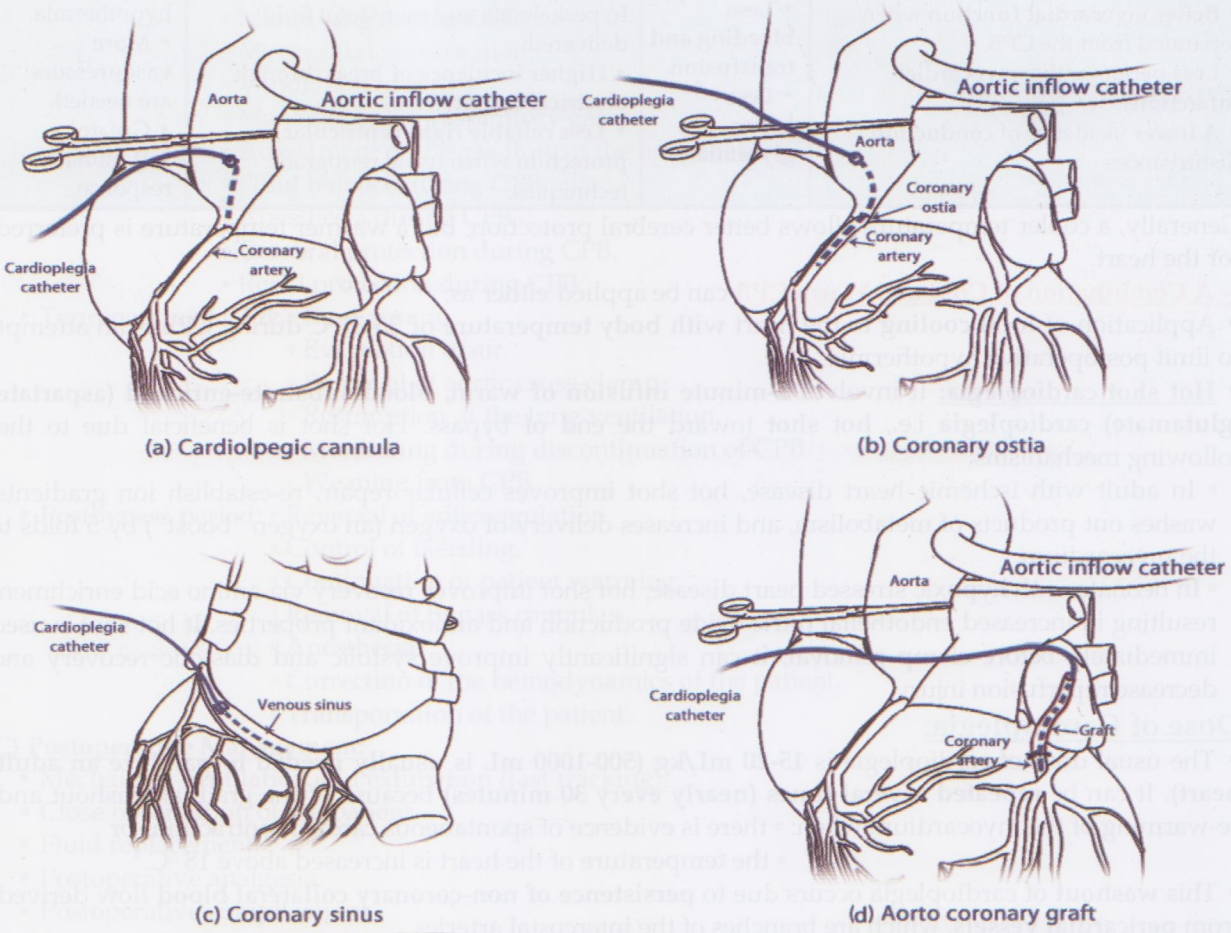


Figure 25-10: Method of administration of cardioplegia

Proper positioning of the coronary sinus catheter may be confirmed by:

- **Monitoring of coronary sinus pressure** during retrograde administration. If the pressure at the distal tip of the coronary sinus catheter during cardioplegia administration at a 200-mL/min infusion is **40-60 mmHg**, the catheter is **correctly positioned**, but if the pressure is **equal to central venous pressure**, the catheter is not in the coronary sinus, but is most likely **in the right atrium**. If the pressure is **very high (> 100 mmHg)**, the coronary sinus catheter is up **against a vascular wall**.
- **Trans-esophageal echocardiography**.

- **Manual palpation** by the surgeon.

Malposition of the coronary sinus catheter e.g., too distally placed, compromises delivery of cardioplegia solution to the right ventricle and results in poor right ventricular protection.

Temperature of Cardioplegia Solution:

a- Cold Cardioplegia: It is the most commonly and traditionally used. Cardioplegia is stored at **4°C.**

b- Normothermic (Warm or Tepid) Cardioplegia:

It was started in the late 1980s and early 1990s. It is used at a temperature of **> 33 °C**. It is thought to be superior to cold cardioplegia, and it is usually given **continuously rather than intermittently**.

Advantages		Disadvantages	
Cardiac	Non-cardiac	Cardiac	Non-cardiac
• More reliable return to **sinus rhythm** without requiring defibrillation. • More homogenous **distribution** of cardioplegia to the left ventricle, because it is applied by a retrograde infusion technique via the coronary sinus especially with severely obstructive coronary artery disease. • **Better myocardial function** when separated from the CPB. • **Less** perioperative myocardial **infarctions**. • **A lower** incidence of **conduction** disturbances.	• **Shorter CPB time.** • **Faster extubation.** • **Shorter intensive care unit time.** • **Less bleeding and transfusion.** • **Less hyper-glycemia.**	• Needing **continuous (usually retrograde)** cardioplegic flow. • **Visual obscurement of the surgical field** during arterial anastomosis as the field is not bloodless. • **Greater infusion volumes** of hyperkalemic hemodiluted cardioplegic solution that results in more hyperkalemia and more total fluid delivered. • **Higher incidence of breakthrough electrical activity.** • **Less reliable right ventricular protection** when using retrograde techniques.	• **Loss of cerebral protection;** therefore, the incidence of stokes increases 3 folds due to absence of hypothermia. • **More vasopressors** are needed. • **Greater inflammatory** response.

Generally, a cooler temperature allows better cerebral protection, but a warmer temperature is preferred for the heart.

c- A Combination of Cold and Warm CPB can be applied either as:

• Application of **local cooling** to the heart **with body temperature of 33-37°C** during CPB is an attempt to limit postoperative hypothermia.

• **Hot shot cardioplegia:** It involves **5-minute infusion of warm, blood substrate-enriched (aspartate /glutamate) cardioplegia** i.e., **hot shot** toward the end of bypass. Hot shot is beneficial due to the following mechanisms:

- In adult with ischemic heart disease, hot shot improves cellular repair, re-establish ion gradients, washes out products of metabolism, and increases delivery of oxygen (an oxygen "boost") by 5 folds to the myocardium.
- In neonate with hypoxic stressed heart disease, hot shot improves recovery via amino acid enrichment resulting in increased endothelial nitric oxide production and antioxidant properties. If hot shot is used immediately before clamp removal, it can significantly improve systolic and diastolic recovery and decrease reperfusion injury.

Dose of Cardioplegia:

• The usual dose of cardioplegia is **15-20 mL/kg (500-1000 mL is usually needed to paralyze an adult heart).** It can be **repeated several times (nearly every 30 minutes)** because of the gradual washout and re-warming of the myocardium when:
- there is evidence of spontaneous cardiac contractions or
- the temperature of the heart is increased above 18 °C.

• This **washout** of cardioplegia occurs due to **persistence of non-coronary collateral blood** flow derived from **pericardial vessels,** which are branches of the intercostal arteries.

• Multiple doses of cardioplegia solutions may improve myocardial preservation by preventing the excessive build-up of metabolites that inhibit anaerobic metabolism.

• **Excessive cardioplegia** may produce:
- Absence of electrical activity.
- Atrio-ventricular conduction block due to intra-myocardial hyperkalemia. This heart block usually resolves in 1-2 hours and can be treated by a temporary artificial cardiac pacemaker.
- A poorly contractile heart at the end of bypass.
- Persistent systemic hyperkalemia, which necessitates insulin-glucose infusion or a hemoconcentrator.

Ca^{++} administration partially offsets these effects, but excessive Ca^{++} increases myocardial damage.

Anesthetic Management of Cardiac Surgery

The anesthesiologist must follow the progress of the surgery and anticipate problems associated with each step because surgical manipulations often have a profound impact on circulatory function.

Anesthetic management of cardiac surgery includes:

A) Preoperative Management:

- Preoperative evaluation and assessment.
- Premedication.
- Patient preparation.
- Patient monitoring.

B) Intraoperative Management:

- Induction of anesthesia.
- Maintenance of anesthesia.
- Prebypass period:
  - Hemodynamic changes.
  - Cannulation for CPB.
  - Bleeding prophylaxis.
  - Anticoagulation.
- Bypass period:
  - Initiation of CPB.
  - Pump flow and mean arterial blood pressure.
  - Monitoring during CPB.
  - Myocardial preservation.
  - Ventilation of lungs.
  - Management of respiratory gases.
  - Adjustment of the gas flow of the oxygenator.
  - Fluid balance during CPB.
  - Anesthesia during CPB.
  - Cerebral protection during CPB.
  - Renal protection during CPB.
- Termination of CPB:
  - Re-warming.
  - Evacuation of air.
  - Removal of aortic cross-clamp.
  - Resumption of the lung ventilation.
  - Monitoring during discontinuation of CPB.
  - Weaning from CPB.
- Postbypass period:
  - Reversal of anticoagulation.
  - Control of bleeding.
  - Continuation of patient warming.
  - Removal of bypass cannulas.
  - Anesthesia.
  - Correction of the hemodynamics of the patient.
  - Transportation of the patient.

C) Postoperative Management:

- Mechanical ventilation and extubation (fast tracking).
- Close observation of the patient.
- Fluid replacement.
- Postoperative analgesia.
- Postoperative complications.
- Anti-platelet therapy.

Preoperative Management

1) Preoperative Evaluation and Assessment

- Careful assessment of **cardiovascular system** is essential such as assessment of hypertension, angina, and left ventricular function; orthopnea, paroxysmal dyspnea, exercise tolerance, and cardiovascular investigations such as ECG, echocardiography (trans-thoracic or trans-esophageal), and coronary angiography. The details of preoperative assessment are discussed in chapter "Cardiovascular Disease".

- Measurement of the **body weight and height** is needed.
- Assessment of **other systems** e.g., pulmonary, central nervous system, renal…etc is also important.
- There are many **risk scoring** that are used for patients undergoing cardiac surgeries such as:

a- Cardiac Anesthesia Risk Evaluation (CARE) Scale:

The cardiac anesthesia risk evaluation scale (CARE score) is a simple risk classification system for patients undergoing cardiac surgery. This can rapidly stratify a patient for the probability of morbidity and mortality.

Parameters	Status	Group
Cardiac Disease	Stable	A1
	Uncontrolled	A2
	Advanced (end stage)	A3
Medical Diseases	None	B1
	1 or more controlled	B2
	1 or more uncontrolled	B3
Cardiac Surgery	Noncomplex	C1
	Complex	C2
	Undertaken as last hope to save or improve life	C3
Urgency of Surgery	Not emergency	D1
	Emergency (surgery performed as soon as diagnosis is made and an operating room is available)	D2

b- Parsonnet Risk Stratification Scheme:

The Parsonnet risk stratification scheme can be used to score the risk and predict the mortality rate in cardiac surgical patients. However, it should only be used as a guide to surgical outcome.

Risk Factor	Score
Female gender	1
Age 70-74	7
> 75	12
Ejection fraction: Good	0
Fair (30-49%)	2
Poor (< 30%)	4
Obesity: > 1.5 times ideal weight	3
Diabetes	3
Hypertension: systolic > 140 mmHg	3
Re-operation: First re-operation	5
Second or subsequent operation	10
Preoperative intra-aortic balloon pump: present for surgery	2
Left ventricle aneurysm	5
Valve surgery: mitral: Pulmonary artery pressure < 60 mmHg	5
> 60 mmHg	8
Valve surgery: aortic: gradient < 120 mmHg	5
> 120 mmHg	7
Valve and CABG	2
Emergency surgery following cardiac catheter	10
Dialysis dependent	10
Catastrophic states	10-50
Other circumstances (asthma…etc)	2-10

Score	Risk	Predicted Mortality
0-4	Good	1%
5-9	Fair	5%
10-14	Poor	9%
15-19	High	17%
> 20	Very high	31%

2) Premedication

1- Sedative Hypnotics:

• The most important thing is to make a **preoperative visit** to the patient for full explanation and reassurance.

Generally, ▫ Relatively **heavy premedications** are required for patients **with coronary artery disease**.
▫ Relatively **light premedications** are required for patients **with valvular diseases** (who are often physiologically dependant on increased sympathetic tone).
▫ **Relatively light premedications** are required in patients with **poor cardiac reserve** or those with underlying **pulmonary disease**.

• O_2 supplementation 2-3 L/min via a nasal cannula is useful in avoiding hypoxemia after premedication.

• For example: ▫ Midazolam 5-10 mg i.m, diazepam 5-10 mg oral, or lorazepam 2-4 mg oral alone or with morphine 5-10 mg i.m.
▫ Morphine 0.1-0.15 mg/kg i.m. with Scopolamine 0.2-0.3 mg i.m. Scopolamine should be avoided in patients > 70 year old as it is associated with a high incidence of confusion.

2- Anticholinergics are better **avoided.**

3- Preoperative Therapy:

• All **antianginal and antihypertensive** treatment such as propranolol should be **continued till the time of surgery.**

• **Digitalis** should be stopped **for one-half life before CPB** i.e., 1.5-1.7 days for digoxin or 5-7 days for digitoxin because the acid-base and electrolytes disturbance occurring with CPB may predispose to digitalis toxicity. If the patient with congestive heart failure, is digitalis dependent, stop digitalis only the night before the surgery, and avoid predisposing factors especially hypokalemia and hypercalcemia.

3) Patient Preparation

1- **The anesthetic plan** should be clearly prepared and should not be too rigid; therefore, if a problem is encountered with one technique, the anesthesiologist should be ready to change to another immediately.

2- **Adequate preoperative drugs and equipment** should be already prepared as there is little time intraoperatively to search for drugs or equipment. Ideally one vasodilator and one inotrope infusion solution should be mixed and prepared for use before the start of the procedure.

3- The anesthesia machine, monitors, infusion pumps, and blood warmers should all be **checked** before the patient arrives.

4- **The cardioplegia solution** should be prepared and **stored at 4°C.**

5- **Venous access:** While the patient is awake but sedated, **an O_2 mask or nasal cannula** is applied and the patient is connected to a **pulse oximeter**. Cannulation is done as follows:

a- Peripheral Vein Cannulation: a **14 or 16 gauge** i.v. catheter (cannula) is used.

b- Central Vein Cannulation: **(sometimes it is inserted after induction of anesthesia)**

A central venous line is inserted in internal jugular (or subclavian) vein by 2-3 single lumen 14-16 gauge catheters or multi-lumen i.v. catheters. The lumen should be marked as:

- one i.v. port should be dedicated for drug infusions and nothing else (to decrease the dead space),
- another i.v. port for drug boluses, and
- another i.v. port for central venous pressure monitoring.

6- **Blood** should be **available** as an inadvertent injury of the right ventricle may occur during midline sternotomy **especially** if the patient has **a previous midline sternotomy (i.e., a redo)** because the right ventricle may be adherent to the sternum.

4) Monitoring

Most monitors are applied before the induction of anesthesia because this period represents one of the major hemodynamic stresses of the procedure, but some monitors should be inserted after induction of anesthesia, as their application is painful and stressful. The monitors should be displayed on a screen visible to both the surgeon and anesthesiologist. Monitors include:

1- A 5-Lead ECG: (before induction of anesthesia)

- Combined **lead II** (for rhythm) **and V5** (for anterior ischemia) are usually used.
- **Computerized ST segment analysis** is now available.
- **Baseline tracings of all leads** should be recorded on a paper for further reference.

2- Arterial Blood Pressure Monitoring: (before induction)

a- **Non-invasive blood pressure monitoring** should be done for **comparison with invasive blood pressure**.

b- **Invasive Blood Pressure Monitoring:** is applied under local anesthesia while the patient is awake, by an arterial cannula in the radial artery usually; other sites e.g., ulnar, brachial, or femoral can be used.

Precautions if the radial artery is used:

- Use the non-dominant hand (usually the left).
- Using the left radial artery may occasionally give false low readings after sternal retraction due to compression of the subclavian artery between the clavicle and the first rib.
- Avoid using the radial artery on the side of brachial artery cut-down (for cardiac catheterization) because this is associated with high incidence of arterial thrombosis and wave distortion.
- Communication with the surgeon is very important to avoid using the radial artery if it will be used as a graft for CABG.

3- Central Venous Pressure Monitoring: (before or after induction)

It is routine in all patients. It can be inserted in:

- Internal jugular vein that is the preferred site for central venous cannulation.
- Subclavian or external jugular veins especially in the right side because left sided ones are prone to kinking after sternal retraction.

4- Pulmonary Artery Catheter: (before or after induction)

It is **not routinely** used and is only **indicated in** patients with:

- **Compromised ventricular function (ejection fraction <40-50%).** In these patients, the central venous pressure does not correlate with the pulmonary capillary wedge pressure; therefore, pulmonary artery pressure monitoring is indicated. In patients with good left ventricular function, central venous pressure correlates well with the pulmonary capillary wedge pressure; therefore, there is no need for pulmonary artery catheter.
- **Pulmonary hypertension.**
- **Complicated surgical procedure** e.g., combined CABG with valve diseases.

Pulmonary artery catheter **often migrates distally during CPB** and may spontaneously wedge without balloon inflation. Inflation of the balloon under these conditions can rupture a pulmonary artery and cause lethal pulmonary hemorrhage. When a pulmonary artery catheter is used, it should be **routinely pulled back slightly (2-3 cm) during CPB** and the balloon subsequently inflated slowly. If the catheter wedges with less than 1.5 mL of air in the balloon, it should be pulled back further.

The values of invasive arterial blood pressure, central venous pressure, and pulmonary artery catheterization is discussed in more details in the chapter of "Monitoring for Anesthesia & Intensive Care".

5- Urine Output (after induction of anesthesia)

A urinary catheter is inserted after the patient is anesthetized because it is very stressful to the patient. Sudden appearance of **red urine** may indicate excessive hemolysis due to CPB itself or due to a transfusion reaction.

6- Temperature: (after induction of anesthesia)

- Multiple probes are inserted after the patient is anesthetized to measure:
  - Rectal or bladder temperature, which represents average body temperature.
  - Esophageal or nasopharyngeal temperature, which represents core temperature.

Multiple probes are needed:

- **Because core-peripheral temperature gradients** give some guide to peripheral perfusion.
- To estimate the **average temperature**.
- To achieve **even distribution of the body temperature** because:
  - During cooling and re-warming using the pump oxygenator, the esophageal temperature changes rapidly whereas, the rectal temperature changes slowly.
  - During surface cooling and re-warming, the rectal temperature changes quickly while the esophageal temperature changes slowly.

- **Myocardial temperature** is usually measured directly during CPB; **10-15 °C** is considered desirable.

7- Laboratory Monitoring: (after induction of anesthesia). It includes:

- Arterial blood gases (every 30 minutes), hematocrit, serum K^+, Ca^{++}, glucose, and Mg^{++}.
- **Thrombo-elastography**: It assesses the visco-elastic changes in the blood during clotting.

- **Activated Clotting Time (ACT):**
  - 2 mL of blood are put into a test tube containing **celite** to activate coagulation. The tube is kept at 37 °C and clot formation is watched or indicated by the presence of **a magnet in the tube**, which is fixed by the machine (**Hemochron apparatus**). The tube rotates in the machine; so, on clot formation, the magnet rotates also stimulating an alarm (figure 25-11).
  - ACT is measured **before** heparin administration (baseline), **3-5 min after** heparin administration and **at a 30-60 min interval** thereafter.
  - ACT prolongation occurs within 1 min after heparin bolus injection, although the heparin peak action occurs 10-20 minutes after administration. This is because of an artifact from hemodilution and hypothermia, which prolongs the ACT.

  Values:
  - Normal ACT value = 90-120 sec (or < 130 sec).
  - **Most centers keep ACT values > 400-480 sec (i.e., triple the normal)** before starting the bypass.

  A heparin dose-response curve can be obtained (see later).



Figure 25-11: An ACT tube where the celite and the magnet appear at the bottom of the tube

8- Surgical Field Monitoring: (after induction of anesthesia)

- **Blood loss and surgical maneuvers** must be closely watched and related to changes in hemodynamics and rhythm.
- Once the sternum is opened, lung expansion can be seen via the pleura.
- Once the pericardium is opened, the heart (primarily the right ventricle) is visible, so that the cardiac rhythm, volume, and contractility can often be judged visually.

9- Trans-esophageal Echocardiography: (after induction of anesthesia)

It gives information about **cardiac anatomy and function** during surgery. Values, technique, and complications are discussed in the chapter of "Monitoring for Anesthesia & Intensive Care".

10- Electroencephalography (EEG) (especially processed):

EEG is very important to detect **the anesthetic depth and central nervous insult**.

Disadvantages:

- It is affected by anesthetic agents, hypothermia, and hemodilution.
- Most strokes during CPB are due to small emboli; therefore, they are not detected by EEG.
- Artifacts from the CPB roller pump can be seen in the unprocessed EEG, but not in the processed one.

11- Trans-cranial Doppler:

It is used to measure blood flow velocity in the basal arteries of the brain (usually the middle cerebral artery), via the temporal bone, to detect cerebral emboli.

Intraoperative Management

Induction of Anesthesia

Only general anesthesia with controlled ventilation is used. **Slow smooth induction (cardiac induction)** is usually indicated.

a- In Patients with Relatively Good Left Ventricular Function:

Anesthesia is induced with thiopentone 1-2 mg/kg (a small dose), propofol, etomidate, or ketamine, in addition to fentanyl 5-10 μg/kg.

b- In Patients with Poor Left Ventricular Function:

- Anesthesia is induced with **a high dose of opioids** while arterial blood pressure and heart rate are continuously evaluated after loss of consciousness. Avoid excessive pressor response or excessive hypotension.
- After induction, a nasal or oral airway, urinary catheter, rectal temperature probe and finally a tube is inserted.
- Muscle relaxants used are either:
  - Succinylcholine, if difficult intubation is suspected.
  - Non-depolarizing muscle relaxants especially agents with little or no cardiovascular effects such as: rocuronium, cis-atracurium, vecuronium, doxacurium, or pipecuronium. Pancuronium is of choice with high dose opioids due to its vagolytic effect, which offsets the induced bradycardia of opioids.
- After intubation and controlled ventilation, baseline investigations are done such as ACT (normal < 130 sec), arterial blood gases, hematocrit, serum electrolytes…etc.

Maintenance of Anesthesia

a- In Patients with Relatively Good Left Ventricular Function:

(i.e., with ejection fraction > 40-50%): Two methods can be used:

I) Mixed Intravenous/Inhalational Anesthesia:

An inhalational agent is used with an intravenous agent such as opioids, low-dose infusion of propofol 25-50 µg/kg/min, or remifentanil. The concentration of inhalational agent is increased slowly and carefully titrated to the arterial blood pressure.

Halothane, isoflurane (in spite of theoretical possibility of coronary steal phenomenon; in animal not in human), enflurane, sevoflurane, or desflurane are used successfully during cardiac surgery.

N_2O is avoided due to its tendency to expand any intravascular **air bubbles** during CPB and if it is used, it should be discontinued 10-20 min before CPB.

Advantages:

- The ability to change the anesthetic concentration rapidly.
- Volatile agents have preconditioning protective effects on ischemic myocardium.
- Recent volatile agents such as sevoflurane or desflurane allow less myocardial depression than older agents and allow fast-track management.

Disadvantages:

- Inhalational agents produce dose-dependent direct myocardial depression.

II) Total Intravenous Anesthesia (TIVA):

It uses short-acting agents such as:

- propofol 0.5-1.5 mg/kg followed by 25-100 µg/kg/min, and
- remifentanil 0-1 µg/kg followed by 0.25-1 µg/kg/min.

Target controlled infusion (TCI) can also be used with propofol maintaining a target plasma concentration of **1-2 µg/mL** that is chosen for **high-risk patients,** and is **increased in small steps** (**0.5-1µg/mL**) until the desired effect is reached.

1200

Advantages:

- TIVA with short acting agents allows "fast-track management".

b- In Patients with Poor Left Ventricular Function:

(i.e., with ejection fraction < 40-50%)

TIVA is the most commonly used. It is either:

I) High Dose Opioid:

Fentanyl, sufentanil, and remifentanil are the most commonly used drugs. A small dose of benzodiazepines or barbiturates can be added.

	Fentanyl	Sufentanil	Remifentanil
Induction	10-40 µg/kg	5-10 µg/kg	0.5-1 µg/kg
Maintenance Infusion	0.3-1.0 µg/kg/min	0.075 µg/kg/h	0.1-1 µg/kg/h
Maintenance Boluses	1-5 µg/kg every 30 min	0.25-1 µg/kg	0.25-1 µg/kg

Advantages: Opioids produce hemodynamic stability (some cardiac depression and vasodilation may occur with sufentanil in elderly patients).

Disadvantages:

1- Patient awareness is common; therefore, concomitant use of benzodiazepines or low dose volatile agents is needed.

2- Poor control of the hypertensive response to stimulation; therefore, vasodilators (nitroglycerin or nitroprusside), β blockers (esmolol), or volatile agents are used.
3- Narcotic induced bradycardia.
4- Narcotic induced muscle rigidity; therefore, muscle relaxants should be given as soon as consciousness is lost e.g., small dose pancuronium.
5- Narcotic induced respiratory depression. It is not a problem because nearly all patients are ventilated postoperatively.

II) Combination of Ketamine and Midazolam:

This combination can be used for induction and maintenance. They are compatible. They can be mixed in the same syringe or solution bag (in a ratio of 20 ketamine: 1 midazolam).

- For induction: ▫ Ketamine 1-2 mg/kg slow i.v. bolus.
  + ▫ Midazolam 0.05-0.1 mg/kg slow i.v. bolus.
- For maintenance: ▫ Ketamine 20-60 μg/kg/min i.v. infusion.
  + ▫ Midazolam 1-3 μg/kg/min i.v. infusion.

Advantages:
1- Relatively stable hemodynamics. It is best for patients with poor left ventricular function.
2- Good amnesia.
3- Good analgesia.
4- Minimal postoperative respiratory depression.
Disadvantages: Significant hypertension with surgical stimulation may occur; therefore, it requires a vasodilator or a low dose volatile agent.

Prebypass Period (i.e., after induction and before CPB)

Anesthetic problems include:

1- Hemodynamic Changes:

Hemodynamic changes may occur during this period:

- **Periods of minimal stimulation** including skin preparation and draping, result in hypotension.
- **Periods of maximal stimulation** including skin incision, harvesting of arterial and venous grafts, sternotomy, sternal retraction, opening the pericardium and sometimes, aortic dissection, result in tachycardia and hypertension, which necessitate adjusting the anesthetic depth. During sternal splitting, stop ventilation and deflate the lungs to avoid lung injury from the electric saw.
- **Accentuated vagal responses.** Marked bradycardia and hypotension may occur during sternal retraction or opening of the pericardium especially if the patient is on β blockers, diltiazem, or verapamil.
- **Deeply anesthetized patients** have a progressive **decrease in cardiac output** after the chest is opened due to decreased venous return as the normally negative intra-thoracic pressure becomes atmospheric; this needs i.v. fluids.
- **Myocardial ischemia** may occur due to hemodynamic changes (increased or decreased arterial blood pressure and heart rate); therefore, a prophylactic nitroglycerin infusion 1-2 μg/kg/min is required (controversial).

2- Cannulation for CPB:

a) Arterial (Aortic) Cannulation	b) Venous Cannulation
Site: in the **ascending aorta**. An aortic cross-clamp is placed between the antegrade cardioplegia catheter and the arterial inflow catheter to separate the heart from the circulation and allow cardioplegia arrest.	**Site:** in the right atrium usually through **the right atrial appendages.**
It should be **done first** (before venous cannulation) because: • Venous cannulation is associated with hemodynamic problems. • Rapid fluid infusion can be given via the aortic cannula to the patient if necessary.	It should be **done after** arterial cannulation.

Precautions:	Precautions:
• The cannula should be **positioned properly** as mal-position results in aortic dissection, and preferential flow of the blood to the innominate artery occurs during CPB; therefore, some clinicians advocate decreasing the **systolic arterial blood pressure to 90-100 mmHg** to facilitate placement of the aortic cannula. • **Air bubbles** should be **completely removed** from the arterial cannula to avoid air emboli into the coronary or cerebral circulations; therefore, some clinicians advocate **temporary compression of the carotid artery** during aortic cannulation to decrease the likelihood of cerebral emboli.	• The cannula should be **positioned properly** as mal-position results in interference with venous return, which may result in poor venous return to the reservoir on initiation of CPB. For example, ▫ Insertion of a cannula too far into the superior vena cava can obstruct the right innominate vein and lead to an increase in the cerebral venous pressure with associated cerebral and facial edema (eyes and sclera). ▫ Insertion of a cannula too far into the inferior vena cava results in abdominal vascular distension. Confirmatory evidence of misplacement of a vena cava cannula is inadequate venous return from the patient to the CPB machine. Prompt withdrawal of the vena cava cannula to a more proximal position should immediately improve venous drainage. • **Hypotension** can occur due to impaired ventricular filling, which occurs during manipulation of the venae cavae and the heart. • It precipitates **arrhythmias** such as premature atrial contractions, supraventricular tachycardia, atrial fibrillation (resulting in hemodynamic deterioration), and ventricular arrhythmias (rare).

3- Bleeding Prophylaxis:

• Bleeding prophylaxis with antifibrinolytic agents may be initiated before or after anticoagulation. Some clinicians prefer to administer antifibrinolytic agents after heparinization to reduce the possible incidence of thrombotic complications; delayed administration may reduce their efficacy. The agents used for bleeding prophylaxis include aprotinin, tranexamic acid, or epsilon-amino-caproic acid (EACA).

• Aprotinin may increase the incidence of renal failure, myocardial infarction, heart failure, stroke, or encephalopathy due to its antifibrinolytic action. Consequently, the use of aprotinin in coronary bypass surgery has markedly decreased and its routine use in cardiac surgery is not recommended. On the other hand, aprotinin may be beneficial in high-risk patients undergoing procedures such as complex valvular replacement, reoperation, aortic surgery requiring deep hypothermic circulatory arrest, and in patients with bleeding disorders or belonging to the Jehovah's Witness religious group.

• These drugs are discussed in more details in chapter "Pharmacological Adjuncts to Anesthesia & Intensive Care". Both intraoperative normovolemic hemodilution and intraoperative plasmapheresis can be used.

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4- Anticoagulation:

Values: It is done before CPB to: • prevent acute disseminated intravascular coagulation and
• prevent formation of clots in the pump.

Method:

Heparin is used to produce anticoagulation. It is given by one of the following:

a- The anesthesiologist: **300-400 unit/kg (3-4 mg/Kg)** is given via a central line (heparin ampoule (1 mL) = 50 mg = 5000 IU). It is usually given while the aortic purse string sutures are placed during cannulation.

b- The surgeon: directly into the right atrium.

c- Recently, **coated circuits** are used with either heparin or other substances: It has the following advantages:

- It reduces the inflammatory response to CPB. Markers of leukocyte activation and complement activation are decreased.
- It has lower incidence of atrial fibrillation.
- It has lower incidence of bleeding.

Confirmation of the Adequacy of Anticoagulation: is performed by one of the following methods:

1- The Activated Clotting Time (ACT):

• It is the one most commonly used. It is measured **before heparin** administration to get a baseline value. It is measured **3-5 min after heparin** administration. It should be **> 400-450 sec** (most centers keep **the ACT > 480 sec**). If ACT is < 400 sec, additional heparin 100 units/kg should be given.

• If aprotinin has been used, a kaolin ACT is used rather than celite ACT because aprotinin artificially prolongs the celite-activated clotting time (celite-ACT) in presence of heparin; so, this may cause inadequate coagulation during cardiopulmonary bypass. Because aprotinin is a serine protease inhibitor, it interacts with antithrombin III to inhibit the action of all intrinsic and common pathway factors resulting in prolongation of measures of coagulation such as ACT. The kaolin-ACT is better used because it is less affected by aprotinin and it appears that the kaolin activator absorbs 98% of aprotinin from the blood and any intrinsic antithrombin effect that aprotinin has is eliminated. If kaolin-ACT is used with presence of aprotinin, ACT value should be > 480 seconds before bypass. If a kaolin ACT is not available and celite ACT is used, give a fixed heparin dose based on the patient's weight and duration of CPB and the ACT value should be more than 750 seconds before initiation of CPB.

2- The High Dose Thrombin Time (HiTT):

It is unaffected by aprotinin but **it has many disadvantages**:

- It is more complicated to perform than a kaolin-ACT.
- It cannot provide a pre-heparin control.
- It cannot provide an index for the adequacy of reversal with protamine.

3- Heparin Concentration Assays:

It measures heparin level, but not its effect; therefore, it is not reliable for measuring the degree of anticoagulation.

Heparin Resistance:

Cause: Heparin resistance occurs in patients having:

- **Anti-thrombin III deficiency** (acquired or congenital).

  N.B.: Anti-thrombin III is a circulating serine protease that irreversibly binds and inactivates thrombin and other active factors X, XI, XII, XIII. When heparin makes complexes with anti-thrombin III, the latter's anticoagulant activity is enhanced 1000 times; therefore, anti-thrombin III is important for anticoagulation.
- Enhanced factor VIII activity.
- Platelet activation resulting in a decrease in the ACT response to heparin.

Treatment:

- Two units of fresh frozen plasma.
- Anti-thrombin III concentrates.
- Synthetic anti-thrombin III.

Then heparin can act easily.

Patients with History of Heparin-Induced Thrombocytopenia (HIT):

There are two types:

Type I HIT	Type II HIT
• It presents in **10-20%** of patients receiving un-fractionated heparin.	• It presents in less than **<5%**.
• It occurs **1-4 days** after heparin therapy and generally improves despite continuing heparin therapy.	• It occurs **5-10 days after heparin** therapy.
• It is **a mild benign** form of thrombocytopenia (rarely < $100 \times 10^3/\mu L$).	• It is a **severe life-threatening** condition with severe thrombocytopenia (<$50 \times 10^3/\mu L$) with major **thrombo-embolic processes** (arterial thrombosis may cause limb ischemia, cerebro-vascular stroke, or myocardial infarction).
• Due to **pro-aggregatory effects of heparin** on the platelets.	• Due to **heparin dependent antibodies** that agglutinate the platelets. The antibodies will bind to the complex formed between heparin and platelet factor 4 (PF4). This makes the platelets adhere, aggregate, and form platelets clots (white clots), which cause a thrombo-embolic phenomenon in 20% of patients.

Diagnosis of HIT:

1- Heparin-induced serotonin release assay.

2- Specific heparin-induced platelet activation assay to detect heparin/PF4 complex and antibodies.

Treatment oF HIT:

a- If the history of HIT is **remote** e.g., weeks, antibodies can no longer be demonstrated. **Heparin may be used safely**, but only for CPB.

b- If the history of HIT is **recent**:

1- **Change the tissue source of heparin,** as HIT occurs frequently with bovine and porcine heparin.

2- Some types of low molecular weight heparin **(LMWH)** can be used, but there may be a cross-reactivity with un-fractionated heparin.

3- **Ancord** is a de-fibrinogenating agent (from Malayan pit viper). It acts by cleaving fibrinopeptide A from the fibrinogen. Its activity is monitored by plasma fibrinogen concentration.

4- **Plasmapheresis** is used to remove these antibodies transiently then heparin can be used normally.

5- Inactivation of platelets with **aspirin, dipyridamole, prostacyclin (or a prostacyclin analogue e.g., iloprost)** also protects the platelets from the activating effects of the CPB circuit before heparinization for CPB in emergency cardiac surgery.

6- Use **r-hirudin, bi-valirudin, lepi-rudin, or agratroban** instead of heparin for anticoagulation.

These drugs are discussed in the chapter of "Pharmacological Adjuncts for Anesthesia & Intensive Care".

N.B.: **Do not administer platelet transfusion** because it increases the risk of thrombosis.

Bypass Period

1- Initiation of CPB:

Time of Initiation of CPB:

Initiation of the CPB should be done after:
- the cannulas are properly placed and secured.
- the ACT is acceptable.
- the perfusionist is ready.

Some authors advocate **a checklist before initiating CPB**, which includes "HADDSUE":

Heparin.

ACT.

Drugs: muscle relaxants or anesthetics.

Drips: to control blood pressure or venous return.

Swan: pull the Swan-Ganz catheter back 5 cm to avoid pulmonary arterial injury or pulmonary infarctions during bypass.

Urine: should be normal.

Emboli: check the aortic cannula visually to detect any emboli.

Technique of Initiation of CPB:

Clamps placed across cannulas during insertion are **removed** (venous first then arterial). The main CPB pump is started. Observation of **venous return to the pump reservoir** is important, which should be normally adequate, and the reservoir level should rise. CPB pump flow is gradually increased.

Precautions:

1. If the venous return is poor (as shown by a decreased reservoir level), the pump prime will quickly empty and the air may enter the pump circuit; therefore,
   - Check the cannulas for proper placement, forgotten clamps, kinks, or an air lock.
   - The pump flow should be slowed until the problem is resolved.
   - Adding volume (blood or colloid) to the reservoir may be needed.
2. With full CPB, the heart should gradually empty. Failure to do so or progressive distention indicates either:
   - mal-positioning of the venous cannula or
   - aortic regurgitation which needs immediate aortic cross clamping and introduction of cardioplegia.

2- Pump Flow and Mean Arterial Blood Pressure:

a) Pump Blood Flow:

It should be **>70% of the cardiac output,** which is enough to maintain tissue oxygenation and perfusion.

Adequate Values at Normal Temperature are

- Adult: **50-70 mL/kg/min** or **2.2-3.1 L/min/m^2.**

N.B.: Normal cardiac output = 70 mL/kg/min = 3.1 L/min/m^2 body surface area.

- Pediatrics: 100-150 mL/kg/min (higher levels are needed due to presence of higher metabolism) or 2.2-3.1 L/min/m^2 (the same as adult).
- Neonates: 150-175 mL/kg/min.

Adjustment of Pump Flow with Hypothermia:

- Hypothermia decreases O_2 consumption, usually every 7-8 °C decrease in temperature decreases O_2 consumption by 50% (see before); therefore, the pump flow may be decreased proportionally if the blood O_2 content does not change.
- At 30°C (i.e., moderate systemic hypothermia) without hemodilution, the adequate pump flow is 30 mL/kg/min or 1.2 L/min/m^2.

At profound hypothermia, complete circulatory arrest for 60-90 min is tolerable.

Adjustment of Pump Flow with Hemodilution:

- O_2 delivery = cardiac output x arterial O_2 content.

Arterial O_2 content = 1.34 x hemoglobin x O_2 saturation + 0.003 x PaO_2.

- **Hemodilution** decreases **hemoglobin (Hb) concentration** and hence decreases O_2 content. Therefore, to deliver the same amount of O_2, **the pump flow has to be increased accordingly**.

For example, if the hematocrit (Hct) is diluted from 40% to 20% during CPB, the pump flow has to be increased by a factor of 40/20.

Clinically, both hypothermia and hemodilution are applied simultaneously so that the adjustment has to be done at the same time.

For example, the pump flow for adults at a temperature of 30°C and a Hct of 25% will be as follows: 50 to 70 mL/kg/min x 50% x 40/25 = 40 to 56 mL/kg/min.

b) Mean Arterial Pressure (MAP)

MAP = pump flow x systemic vascular resistance.

With constant systemic vascular resistance, MAP is proportional to the pump flow. Also with constant pump flow, MAP is proportional to systemic vascular resistance. Therefore, by controlling systemic vascular resistance and pump flow, MAP can be controlled.

MAP should be maintained between **50-80 mm Hg.** The desirable blood pressure during bypass is debatable. Lower pressures may reduce cerebral blood flow and increase risk of infarctions, but they also reduce the embolic load to the brain per unit time. The reverse occurs when higher blood pressure is applied.

Adjustment of MAP during CPB:

1- At the Onset of CPB:

The MAP usually decreases abruptly, and may reach **30-40 mm Hg** in the first 5-10 min of bypass due to the following:

- **Abrupt hemodilution** decreases blood viscosity, which decreases systemic vascular resistance (this effect is partially compensated by hypothermia, which increases blood viscosity again).
- **Inadequate pump flow at the beginning** of the bypass.
- **Hypoxic vasodilation** from initial perfusion with blood-free primes carrying no O_2.
- **Vasodilation from vasoactive materials released** due to the initial reaction of the serum proteins, red blood cells, and platelets with the foreign surface of the heart-lung machine.
- **Decreased plasma levels of catecholamines** by hemodilution.
- **Nitroglycerin containing cardioplegia** (if used).

2- During Hypothermia in Patients without Increased Risk of Neurological Insult:

Keep **the MAP as low as 30 mm Hg (and the pump flow rate at 30 mL/kg/min).** In practice, higher values are used as a safe guard. **Avoid a higher MAP > 70 mm Hg** because it increases the non-coronary collateral blood flow to the heart via the pericardium and pulmonary venous drainage. Such collateral flow of relatively warm blood tends to wash the colder cardioplegic solution out of the heart and decreases the hypothermic protection against myocardial ischemia.

3- During Hypothermia in Patients with Increased Risk of Neurological Insult: e.g., history of cerebrovascular accident, transient ischemic attacks, hypertension, carotid stenosis, advanced age, severe aortic atherosclerosis (detected by trans-esophageal echocardiography), we need to keep **the MAP at higher levels, between 80-100 mm Hg i.e., above 50 mm Hg during CPB.**

4- During Deep Hypothermia 20-25 °C:

A MAP around 30 mm Hg is considered adequate for the cerebral blood flow.

5- Some Centers **advocate the use of low flow 40 mL/kg/min and low MAP around 40 mm Hg** due to the following advantages:

- Less bleeding via collaterals back into the heart.
- Less trauma to red blood cells and platelets.
- Less fluid requirement.

But there is a risk of inadequate perfusion.

Correction of MAP:

a- Persistent and Excessive Decrease in MAP (< 30 mm Hg):

1- Search for **a possible cause** and manage it e.g.,

- **A pressure-transducer** error.
- **Aortic dissection**: It is managed by temporarily stopping CPB until the aorta is re-cannulated distally.
- **Poor venous return.**
- **Pump malfunction.**

2- **Increase the pump flow rate.**

3- **Vasopressors** e.g., phenylephrine 0.5 mg increments up to MAP of 50 mm Hg.

b- High MAP (> 150 mm Hg) can cause aortic dissection or cerebral hemorrhage.

When the MAP increases > 100 mm Hg, start management as follows:

1- **Increase the depth of anesthesia** by adding **isoflurane** to the oxygenator inflow gas via a vaporizer in the heart lung machine (the best treatment) or by i.v. agents as thiopental, diazepam, midazolam, droperidol, or large dose narcotics, but they are not effective.

2- **Decrease pump flow**. Some authors do not decrease the pump flow rate as this may cause tissue hypoxia even though the MAP is high.

3- **Vasodilators** e.g., nitroprusside in severe cases.

N.B.: **Factitious hypertension** can occur when the right radial artery is used for monitoring and the aortic cannula is directed towards the innominate artery.

N.B.: **Changes in Blood Viscosity during Hypothermia and Hemodilution:**

- Blood viscosity varies inversely with temperature. A 2% increase in the viscosity occurs with every 1°C decrease in temperature at a hematocrit value of 40%. A decrease in temperature from 37°C to 27°C increases the viscosity about 25%.
- Hemodilution with a balanced salt solution will decrease the blood viscosity. A Decrease in the hematocrit from 40% to 20% at 27°C decreases the viscosity by about 40%. It has been recommended that the hematocrit should be adjusted to the same numerical value as the core body temperature in °C, if blood viscosity is kept approximately constant.

3- Monitoring during CPB:

Besides **the previous monitors**, the following monitors should be observed:

1- Central Venous Pressure (CVP):

During the bypass period, it **should be low or zero** to make sure that there is no obstruction to the venous return from the head. **An increase in central venous pressure** with or without facial edema (eyelids and sclera) may **reflect improper placement** of the vena cava cannula and result in obstruction to venous drainage.

2- Pulmonary Artery Pressure Monitoring (PAP):

During the bypass period, it **should be low or zero** to prevent over-distention of the left ventricle. **An increase in PAP** indicates **malfunction of left ventricular vent** and associated inadequate decompression of the left ventricle.

3- Urine Output:

During the bypass period, urine output should be maintained **above 1 mL/kg/h.**

Additional Monitors needed include:

4- The Pump Flow Rate that should be **adequate** for tissue perfusion and oxygenation.

5- The Venous Reservoir Level that should be closely observed to avoid catastrophic air embolism.

6- Arterial Inflow Line Pressure:

It is always higher than systemic mean arterial blood (recorded from a radial artery or even an aortic catheter). The difference in pressure represents:

- The pressure drop across the arterial filter.
- The arterial tubing and the narrow opening of the aortic cannula.

Inflow pressure **should remain < 300 mm Hg.** A higher pressure may indicate a clogged arterial filter, obstruction of the arterial tubing or cannula, or aortic dissection.

7- Monitoring of Blood Flow: of perfusates (i.e., that flow from the CPB machine to the patient) and venous blood (that flows from the patient to the venous reservoir).

8- Myocardial Temperature.

9- Inline (arterial and venous) O_2 saturation.

10- Inline pH, CO_2 Tension, and O_2 Tension sensors that should be confirmed by a direct measurement.

N.B.: Criteria of Inadequate Flow Rate (Inadequate Perfusion or Hypoxia):

- Low **mixed venous O_2 tension < 30-40 mm Hg** (N = 40-45 mm Hg).
- Low **venous O_2 saturation <70%.**
- Progressive **metabolic acidosis**.
- **Low urine output**.

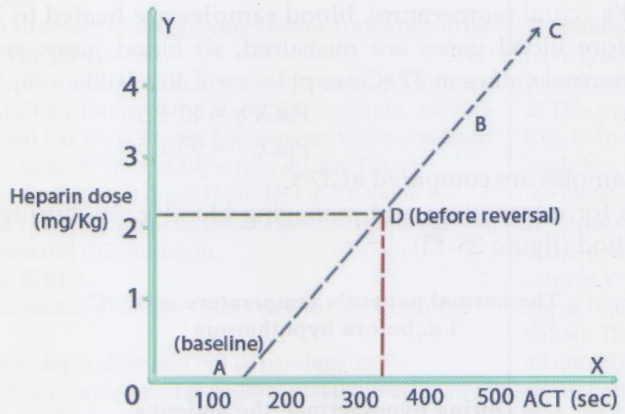
11- Serial ACT:

- ACT should be measured **immediately after the bypass, then every 20-30 min**; thereafter, **extra-heparin is needed if it is < 480 seconds.** Cooling increases $t_{1/2}$ of heparin and prolongs its effect.
- **A heparin dose-response curve** is often used to facilitate calculation of subsequent heparin doses and protamine reversal. Although the relationship does not always conform to a linear function, it remains clinically useful.

1- Plot the initial ACT on the X-axis "A" and the ACT after heparinization "B" and draw a line between (A) and (B).

2- If additional anticoagulation is needed, find the desired ACT on that line (C). The amount of additional heparin needed is the difference on the Y-axis between the present ACT and the desired ACT.

3- For reversal of anticoagulation, measure the ACT before protamine is given (point D). The protamine dose is based on the remaining heparin activity (figure 25-12).



A = Initial ACT
B = ACT after heparin dose
C = Desired ACT after the first heparin dose.
D = Measured ACT before reversal.

Figure 25-12: A heparin dose-response curve

12- Serial Hematocrit:

It is usually kept **between 20 and 25%**; therefore, red blood cell transfusion into the pump reservoir may be needed.

13- Serial Serum K^+, Na^+ and Ca^{++}:

Marked increase in serum K^+ secondary to cardioplegia is usually treated with furosemide.

14- Serial Serum Glucose:

It should be kept **< 250 mg/dL.** Avoid hyperglycemia as it may increase neurological deficits because under conditions of limited cerebral O_2 delivery e.g., during CPB, anaerobic glucose oxidation occurs to provide ATP, which forms lactic acidosis. Therefore, hyperglycemia by providing more glucose increases the degree of intracellular acidosis, which increases the neurological insult.

4- Myocardial Preservation:

Hypothermia and cardioplegia are now applied (see above).

5- Ventilation of the Lungs:

• **After** initiation of **full adequate CPB** and the heart stopping to eject blood, **ventilation is stopped**. Premature discontinuation of ventilation will make any remaining pulmonary blood flow act as a right to left shunt causing hypoxia.

• **Most centers** continue a low flow of **O_2 1-2 L/min** in the anesthesia circuit (± small PEEP 5 cm H_2O) to decrease postoperative pulmonary dysfunction.

• The ventilation is resumed at the end of CPB when the heart begins to eject blood.

6- Management of Respiratory Gases:

• Hypothermia produces ▫ decreased $PaCO_2$ with increasing its blood solubility
▫ decreased PaO_2 with increasing its blood solubility
and ▫ decreased H^+ (i.e., increased pH).

Each degree centigrade below 37°C increases blood pH by 0.015. For example, at 37 °C if pH is 7.40; at 27°C the pH = 7.40 + 0.015 x (37-27) = 7.55 due to increased pKa and decreased $PaCO_2$ because of increased CO_2 solubility in blood during hypothermia.

$$pH = pKa + Log \frac{[HCO_3^-]}{0.03\, PaCO_2}$$

• For example, a blood sample is taken at 37°C, its $PaCO_2$ is 60 mmHg, and its pH is acidotic 7.3 i.e. increased H^+. When this blood sample is cooled to 27°C, its $PaCO_2$ and its pH now after hypothermia will be 40 mmHg and 7.4 respectively; therefore, at 27°C, there will be no management of the excess CO_2 or the acidotic pH.

• Regardless of the patient's actual temperature, **blood samples are heated to 37°C (98.7°F) in the blood-gas analyzer machine** before blood gases are measured, so blood gases are measured at a constant temperature of 37 °C. The normal values at 37 °C are pH = 7.40 ± 0.05
$PaCO_2$ = 40 ± 5
PaO_2 = 95 ± 5

That means all blood-gas samples are **compared at 37°C.**

• There are two strategies for interpreting and managing blood gases during the hypothermia of CPB; pH-stat and alpha-stat method (figure 25-13).

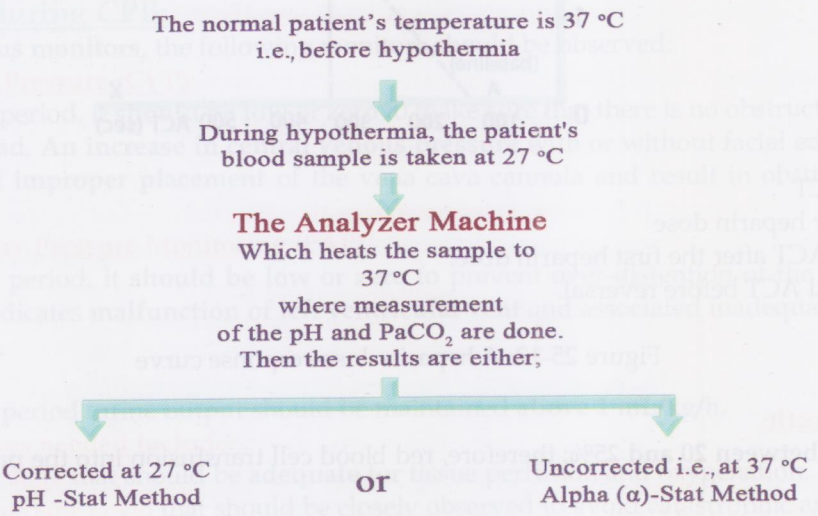


Figure 25-13: pH-stat and alpha-stat methods

If blood gas sample is taken at a patient's temperature 37°C, there is no difference between pH-stat and α-stat management and both give the same results at 37 °C.

• The choice between pH-stat and α-stat management is still controversial, but theoretically, α-stat management is more preferred (see below).

	pH stat (Temperature-Corrected) Method	Alpha-Stat (Temperature-Uncorrected) Method
Idea	In pH-stat, the pH and $PaCO_2$ are measured at 37°C of the machine then the results are corrected **by special tables, nomograms, or by a program in the blood-gas analyzer** to the values at the exact patient's temperature e.g., 27 °C during hypothermia. The patient is treated as if he or she has been a **hibernating animal** (i.e. with changeable body temperature).	In α-stat, the pH and $PaCO_2$ are measured at 37°C of the machine then the results are not corrected regardless of the patient's actual temperature.
Aim	To keep **constant arterial pH at 7.40 and $PaCO_2$ at 40 mm Hg** at any given temperature without keeping $[OH^-]$: $[H^+]$ ratio constant. For example, a blood sample at 27°C (its actual $PaCO_2$ is 40 mm Hg and its pH is 7.4) is taken to the analyzer, which heats the sample to 37°C (its $PaCO_2$ is now 60 mm Hg and its pH is 7.3 as hypothermia decreases $PaCO_2$ and H^+ values). Then the $PaCO_2$ and pH values are corrected to their original values at 27°C i.e., the analyzer's results will be 40 mm Hg and 7.4 respectively. Therefore, this excess CO_2 or acidotic pH will not be detected or managed.	To keep a **constant ratio of $[OH^-]$: $[H^+]$ at about 16: 1** while keeping the pH and $PaCO_2$ at normal uncorrected values. For example, a blood sample at 27°C (its actual $PaCO_2$ is 40 mm Hg and its pH is 7.4) is taken to the analyzer, which heats the sample to 37°C (its $PaCO_2$ is now 60 mm Hg and its pH is 7.3, as hypothermia decreases $PaCO_2$ and H^+ values). Then the analyzer's result will be 60 mm Hg and 7.3 respectively (uncorrected). Therefore, this excess CO_2 and acidotic pH will be detected and managed.
	Disadvantages: 1) This method of measurement increases **CO_2 and H^+** i.e., excess positive charges lead to a change in the state of intra-cellular electro-neutrality (**the intra-cellular state becomes acidotic),** which decreases buffering. Therefore, there is a **change in $[OH^-]$: $[H^+]$ ratio** leading to a **change in the structure and function of the enzyme system and disturbance in normal cellular function.** N.B.: The function and structure of the enzyme system are shown to be optimal at a ratio of $[OH^-]$: $[H^+]$ of 16:1. 2) This method **may require adding CO_2** to the oxygenator gas inflow. This increases **the total CO_2 content** of the blood. For example, a blood sample at 27 °C (its actual $PaCO_2$ is 28 mm Hg) is taken to the analyzer, which heats the sample to 37 °C (its $PaCO_2$ is now 40 mm Hg as hypothermia decreases the $PaCO_2$ value). Then the $PaCO_2$ value is corrected to its original value at 27 °C i.e., the analyzer's results will be 28 mmHg, which necessitates CO_2 addition. 3) **Cerebral blood flow (CBF):** • CBF is close to the normothermic state values due to the effect of excess CO_2. • CBF becomes **pressure-dependent** and not depending on O_2 consumption i.e., CBF is uncoupled to the cerebral metabolism **(cerebral autoregulation is lost).** • pH-stat **increases CBF**, which possibly **increases the embolic load** to the brain (i.e., air/debris). • pH-stat **increases CBF to non-ischemic areas** may cause a steal phenomenon. 4) **Hypothermic protection** of ischemic tissues is **decreased.** 5) **Myocardial function is less preserved.** **Advantage:** 1) Some researches claim that pH-stat management in deep hypothermic cardiac arrest is associated with a better neurological outcome (probably due to increased CBF, which provides better brain cooling and greater cellular O_2 availability) especially **in children.** 2) Acidosis counteracts the leftward shift of the oxygen dissociation curve associated with hypothermia, so that release of O_2 from hemoglobin is enhanced. 3) **Depressed enzymatic activity** associated with acidosis may potentiate the total extent of metabolic depression caused by hypothermia. N.B.: Potentially harmful effects of pH-stat management would seem to outweigh any advantages.	**Advantages:** it is the **most commonly** used. 1) This method of measurement does not increase CO_2 Therefore, there is **no change in the $[OH^-]$: $[H^+]$ ratio** or **in the structure and function of the enzyme system.** 2) This method **does not require adding CO_2** to the oxygenator gas inflow. This leads to a **constant total CO_2 content** of the blood. For example, a blood sample at 27°C (its actual $PaCO_2$ is 28 mm Hg) is taken to the analyzer, which heats the sample to 37°C (its $PaCO_2$ is now 40 mm Hg as hypothermia decreases the $PaCO_2$ value). Then the analyzer's results will be 40 mm Hg (uncorrected), which does not necessitate CO_2 addition. 3) **Cerebral blood flow (CBF):** • It decreases appropriately with the decrease in temperature. • It becomes **pressure-independent** but depends on O_2 consumption i.e., CBF is coupled to the cerebral metabolism **(cerebral autoregulation is preserved).** • Some researches claim that α-stat management in deep hypothermic cardiac arrest is associated with a better neurological outcome especially **in adults.** 4) **Hypothermic protection** of ischemic tissues is **maximal.** 5) **Myocardial function is better preserved.**

7- Adjustment of the Gas Flow of the Oxygenator:

• Normally in the lung, alveolar ventilation is 4 L/min and the pulmonary circulation is 5 L/min; so, the ventilation/perfusion ratio = 0.8 i.e., every one liter of pulmonary blood is ventilated with 0.8 liters of gas.

• **The oxygenator** is not as efficient as human lungs; so, we start with **2 L of gas for each liter of pump flow** rate **then** we adjust the gas flow rate **according to the blood $PaCO_2$ and PaO_2** i.e., the gas flow is decreased if the $PaCO_2$ is low and the PaO_2 is too high. In addition, the gas flow is increased if the $PaCO_2$ is high (> 40 mm Hg) or the PaO_2 is low (< 100 mm Hg).

• **If the bubble oxygenator is used** (as in the past), a **mixture of 99% O_2 and 1% CO_2** is used. This 1% CO_2 is added to **avoid severe hypocapnia,** which is produced due to:

- Decreased CO_2 production during hypothermia.
- Increased CO_2 elimination from the high gas flow.
- Increased CO_2 diffusion capacity.

• Disadvantages of low $PaCO_2$ during CPB:

- **CBF decreases** about 2-4% for each mm Hg decrease in $PaCO_2$, when $PaCO_2$ is in the range of 20-60 mmHg due to cerebral vasoconstriction.
- Respiratory alkalosis **shifts the O_2-dissociation curve to the left**, which increases O_2 affinity to hemoglobin and decreases O_2 release to the tissues.
- **Hypokalemia** occurs due to intracellular shift of K^+ during alkalosis.
- **Decreased ionized Ca^{++}** due to alkalosis.

• **If the membrane oxygenator is used** (it is the most commonly used nowadays), a **mixture of O_2-air** is used. This allows better control of O_2 tension during CPB. Since α-stat regulation is the most common one used, it is not necessary to add CO_2 to the ventilating gas during hypothermia to elevate the $PaCO_2$ and decrease the pH.

8- Fluid Balance during CPB:

• **During CPB, all i.v. lines are shutoff.**

• **The intake (input)** includes:

- **The cardioplegic solution**.
- **Fluid or blood added to the venous reservoir** during CPB. The aim is to maintain hematocrit (Hct) **at least 18-20% during hemodilution**; therefore,
  - If the Hct is decreased <18%, blood is added to the oxygenator.
  - If the Hct is increased >20%, normal saline is used.

  However, Hct between 15-18% appears to be well tolerated clinically.
- **The decreased blood level in the venous reservoir.**

• **The output** includes:

- **Urine output.**
- **The increased blood level in the venous reservoir.**
- **Blood loss.**

9- Anesthesia during CPB:

There is a risk of awareness and hypertension (due to light anesthesia) during CPB especially during re-warming. Anesthesia is maintained by one of the following methods while the patient is on the CPB.

a- Low Doses of Volatile Agents (Isoflurane or sevoflurane) via the Oxygenator:

It should be generally discontinued just before termination of the bypass to avoid residual myocardial depression. Patients with poor left ventricular function may be very sensitive to the combined residual effects of cardioplegia and volatile agents.

b- Additional Doses of Narcotics, Benzodiazepines, Propofol, or Thiopental:

These i.v. agents are preferred in patients with poor left ventricular function. I.v. agents are diluted by the primary solution during CPB, but hypothermia itself produces anesthesia and prolongs the action of i.v. agents by decreasing hepatic metabolism and urinary excretion.

At the end of CPB, some clinicians routinely give:
- midazolam 5-10 mg i.v.,
- scopolamine 0.2-0.4 mg,
- opioid infusion, or
- ketamine-midazolam infusion.

Additional Doses of Muscle Relaxants:

Muscle relaxants are needed to prevent:

- diaphragmatic movement that interferes with the surgery and
- shivering during hypothermia, which increases O_2 consumption.

The **effect of CBP on anesthetic drugs and muscle relaxants** is discussed above.

N.B.: Sweating during re-warming is common and does not necessarily reflect light anesthesia, but rather a hypothermic response to perfusion with blood that is often at 39°C.

10- Cerebral Protection during CPB:

1) Adjust the Pump Flow and Mean Arterial Blood Pressure as before.

2) Avoid Cerebral Emboli with CPB:

1- Use **membrane oxygenators** instead of bubble oxygenators.

2- Use **centrifugal pumps** instead of roller pumps.

3- Use **filters** in the suction line (to remove debris from the blood suctioned from the operative field) and in the arterial line (to remove accidentally introduced air, micro-bubbles, or debris).

4- **Meticulous removal of air** is essential before allowing the blood to be ejected from the left ventricle to the systemic circulation.

5- **Minimal manipulations of the ascending aorta.**

6- **Temporary bilateral external compression of common carotid arteries** by the anesthesiologist when ventricular ejection begins may divert air and debris to other vascular beds.

7- Many clinicians advocate **a head-down position** while intra-cardiac air is being evacuated.

3) α-Stat (Temperature Un-corrected) Method is Preferable because it preserves cerebral autoregulation (the CBF is coupled to cerebral metabolic rate of oxygen).

4) Avoid Hyperglycemia during CPB:

Under conditions of limited cerebral O_2 delivery, anaerobic glycolysis becomes the primary method of ATP production leading to intracellular lactic acidosis. Therefore, hyperglycemia provides more glucose for anaerobic glycolysis. This increases the degree of intracellular acidosis, which correlates with the severity of subsequent cerebral injury.

N.B.: Blood sugar levels are elevated during CPB. This is due to marked elevation of catecholamine levels during CPB, which results in:

- Catecholamine inhibition of insulin secretion causing a defect in glucose utilization.
- Catecholamine induced conversion of glycogen to glucose.

5) Prophylactic Thiopental Infusion:

It decreases the neurological sequelae in patients undergoing open cardiac chamber procedures with normothermic CPB (not in patients undergoing closed CABG operations with hypothermic CPB). Therefore, it is used immediately before and during open cardiac chamber procedures.

Its use is controversial because, although it completely suppresses EEG activity, it may **increase the need for inotropic support** upon termination of CPB due to its cardiac action.

6) Complete Circulating Arrest with Deep Profound Hypothermia.

7) Others:

- Corticosteroids (methyl prednisolone 30 mg/kg).
- Mannitol 0.5 gm/kg.
- Phenytoin 10-15 mg/kg.
- Ca^{++} channel blockers as nimodipine.
- N-methyl-D-aspartate (NMDA) antagonist as ketamine.
- Free radical scavengers.
- Cerebroplegia.

11- Renal Protection during CPB:

Normally, renal blood flow (RBF) is autoregulated between a renal artery pressure of 80 and 180 mm Hg. Despite this, it has been demonstrated that a mean arterial blood pressure at as low as 50 mm Hg during hypothermia, hemodilution, and non-pulsatile CPB does not result in post-CPB deterioration of renal function.

The presence of post-CPB ventricular dysfunction and low cardiac output is a major risk factor in the development of post-CPB renal dysfunction and failure. Therefore, renal protection is done by:

1) Avoiding Oliguria:

Oliguria is a sign of renal hypoperfusion and ischemia. Urine output should be assessed every 15 minutes while on CPB. If urine output falls below 0.5 ml/kg/h, the following actions should be performed:

- **Mean arterial blood pressure should be increased to at least 50 mm Hg.** If this fails to increase the urine output or the mean arterial blood pressure is already optimized,

- Start diuresis with:
  - **furosemide:** 0.5-1 mg/kg or
  - **mannitol:** 0.5-1 gm/kg. Volume expansion following mannitol infusion does not present a problem while on CPB.

Obligatory K^+ loss in the urine may result in hypokalemia before termination of CPB, which may require K^+ supplementation.

2) Avoiding and Managing Hemoglobinuria:

The renal threshold for hemoglobin is 100-150 mg/dL. Pink urine is a sign of massive hemolysis.

Hemolysis is associated with:

- The suction apparatus due to frothing, turbulence, acceleration, and shear forces of negative pressures (the main factor).
- Suction of roller pumps (a lesser degree).
- Blood-gas interface oxygenators (a lesser degree).

Therefore, **maintain high output of alkaline urine by forced alkaline diuresis** to prevent renal tubule damage due to precipitation of acid hematin crystals.

Termination of CPB

Termination of CPB is a team effort between surgeon, anesthesiologist, and perfusionist. The aim is to wean the patient from the bypass machine allowing the heart and lungs to re-establish normal physiological function.

Separation from CPB should be **gradual.** **A checklist for weaning from CPB includes "WRMVP".**

Warming,
Rhythm,
Monitor,
Ventilator (confirm that it is turned on)
Perfusion (heart beating, presence of vasodilation).

1- Re-warming:

It should be **gradual**. It usually takes **20-40 minutes** to re-warm a patient from 28°C to 35°C (while cooling from 37°C to 25°C takes only 5-10 min) because:

- During cooling the patient, the initial venous blood temperature is 37 °C and the water temperature of the heat exchanger is 0-4 °C; so, the temperature gradient is 34-37 °C.
- While during re-warming, the water temperature of the heat exchanger is limited to 42°C or less to prevent denaturation and destruction of the blood; so, the temperature gradient is limited to 10 °C or less.

The re-warming should be **complete** i.e., esophageal or nasopharyngeal temperature should be at least 37°C or rectal or bladder temperature should be at least 35°C before separation from the CPB.

Disadvantages of rapid re-warming:

1- It causes a large temperature gradient between well-perfused organs and peripheral vasoconstricted tissues; so, the subsequent equilibrium after separation from the CPB decreases **the core-temperature again.**

N.B.: Infusion of a vasodilator drug e.g., nitroprusside or nitroglycerin by allowing higher pump flows often speeds the re-warming process and decreases large temperature gradients.

2- It causes formation of **gas bubbles** in the blood stream because the solubility of gases rapidly decreases.

3- **Ventricular fibrillation** may occur during re-warming. It is treated by:

- 5-10 joules by an internal defibrillator.
- 1-2 mg/kg lidocaine before removal of the aortic cross clamp.
  1-2 gm $MgSO_4$ before removal of the aortic cross clamping.
- If ventricular fibrillation persists, recheck arterial blood gases, electrolytes, and body temperature.

2- Evacuation of Air from the Heart and any Bypass Graft:

Many clinicians advocate **a head-down position** while intra-cardiac air is being evacuated to decrease the likelihood of cerebral emboli.

Lung inflation facilitates expulsion of the left sided intra-cardiac air by squeezing pulmonary vessels and returning the blood into the left heart.

Trans-esophageal echocardiography is useful in detecting intra-cardiac air.

3- Removal of Aortic Cross-Clamp:

Aortic cross clamping **can last** for **60-120 minutes** with myocardial hypothermia and cardioplegia without coronary perfusion. The shorter the cross-clamping time is, the better the myocardial function will be.
If the cross-clamping time is expected to be prolonged,

- myocardial hypothermia should be maintained and
- coronary perfusion should be considered by a separate pump.

4- Resumption of Lung Ventilation:

It must be started with **100% O_2.** Re-inflation of the lungs requires temporarily **higher than normal airway pressure.** Re-inflation of the lungs should generally be done **with direct visualization** (or through the pleura) because overzealous lung expansion can interfere with internal mammary artery grafts.

5- Monitoring during Discontinuation of CPB:

1) Central Aortic Pressure:

It is **measured directly**. It should be correlated to the radial artery pressure. The aortic pressure usually becomes higher than the radial pressure (i.e., a reversal of the normal systolic pressure gradient). It also can be estimated by **palpation by the surgeon**.

2) Ventricular Volume and Contractility:

It can be estimated **visually.**

3) Filling Pressure (from Central Venous Pressure and Pulmonary Capillary Wedge Pressure):

- In non-surgical patients, there is a significant correlation between pulmonary capillary wedge pressure (PCWP) and left ventricular end-diastolic volume (LVEDV).
- **After CPB**, in the first few hours, there is a **poor correlation between PCWP and LVEDV**. This poor correlation is not explained by changes in systemic or pulmonary vascular resistance, but **is due to acute changes in ventricular compliance**. Although PCWP measuring remains valuable in clinical management to avoid pulmonary edema, it cannot reliably be used as an index of left ventricular preload while attempting to optimize the stroke volume. **Trans-esophageal echocardiography** can accurately assess LVEDV and cardiac contractility.

4) Cardiac Output Measurement:

It is measured by **thermo-dilution** if available.

5) Trans-esophageal Echocardiography (TEE):

It can provide valuable information about chamber volumes, contractility, and valvular function.

6) Laboratory Values:

They must be within acceptable limits. Any abnormalities should be managed such as:

- Acidosis (if pH < 7.2).
- Hypocalcemia (ionized).
- Hyperkalemia (if > 5.5 mEq/L).
- Hematocrit that should be 22-25%.

7) Urine Output and its Color:

Observe the urine color for hemolysis and maintain urine output for renal protection (see before).

8) Heart Rate:

a- A stable rhythm (preferably sinus) must be present.

- Atrio-ventricular pacing may be necessary and confers the benefit of a properly timed atrial systole.
- If a persistent atrio-ventricular block occurs, **serum K^+ should be measured**. If serum K^+ is increased, it can be treated with Ca^{++}, $NaHCO_3$, furosemide, or glucose/insulin.

b- An adequate heart rate (80-100 beats/min) must be present.

- **A slow heart rate** (more dangerous) should be treated by:
  - **Pacing**: Atrial pacing is preferred due to better cardiac output with atrial kick.
    Ventricular pacing may be needed if there is complete atrio-ventricular block.
  - **Inotropic agents.**
- **A rapid heart rate** (less dangerous) e.g., supraventricular tachycardia or ventricular fibrillation should be treated by **internal cardioversion** with 5 to 10 Watt-seconds (joules). If the heart remains in ventricular fibrillation, blood gases, electrolytes, and temperature are rechecked and lidocaine, 1 to 2 mg/kg is administered before repeated DC defibrillation attempts. Mean arterial blood pressure is usually increased to 80 mm Hg. Occasionally, esmolol, metoprolol, and amiodarone are added to treat intractable ventricular fibrillation or tachycardia.

6- Weaning:

- It is accomplished by:
  - releasing the tapes around the vena cava.
  - progressively clamping the venous return line (tubing).

As the beating heart fills, ventricular ejection resumes.

- **Arterial Blood Pressure: The pump flow gradually decreases as arterial blood pressure increases.** Once the venous line is completely occluded, and **systolic blood pressure is judged adequate > 80-90 mm Hg**, the pump flow is stopped and the patient is evaluated. **Arterial blood pressure is the most easily measured index of successful termination of the bypass**, but arterial blood pressure is a derivative of cardiac output and venous return; so, if there is doubt regarding the pump efficacy, cardiac output and venous return should be measured.
- After coming off CPB, the patient is in one of 4 groups:

	Group I Normal	Group II Hypovolemic	Group III Pump Failure (Low Output Syndrome)		Group IV Hyperdynamic
			A) LV Pump Failure	B) RV Pump Failure	
Ventricular function (can be assessed by direct **vision)**	**Vigorous and good** contracting heart.	Either: • **Normal** ventricular function or • **Poor** ventricular function (see below).	**Sluggish, poorly contracting** heart that progressively distends.		**Good** contracting heart and adequate volume.
Filling pressure Central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP)	Normal	Low	CVP: normal or high PAP: high PCWP: high	CVP: high PAP: normal or high PCWP: normal or high	Low
Blood Pressure	Normal	**Low**	**Low**	**Low**	**Low**
Cardiac Output	Normal	Low	**Low**	**Low**	**High**
Systemic Venous Resistance	Normal	**High**	**High**	Normal or high	**Low**
Treatment	No treatment is needed. The patient can be **separated immediately** from the CPB.	**Volume** replacement continues until the left atrial pressure is 12-15 mm Hg. The patient can be **separated** from the CPB **after volume** replacement.	See below	Pulmonary vaso-dilatation + see below	• **Increase the hematocrit** (as it is usually <22%) by **ultra-filtration** (off CPB) or **red blood cell transfusion.** • **Vaso-constrictors** • The patient can be **rapidly separated** from the CPB.

LV = left ventricular RV = right ventricular

In Hypovolemic Patients, to differentiate between good and poor ventricular function:

Give 100 mL aliquots of pump blood infused via the aortic cannula:

- In good ventricular function, both the arterial blood pressure and cardiac output increase with each bolus (if left ventricular filling pressure is < 10-15 mm Hg, most patients have good blood pressure and cardiac output).
- In poor ventricular function, filling pressure increases > 10-15 mm Hg during volume infusion without appreciable changes in arterial blood pressure or cardiac output.

Differential Diagnosis of Primary Pump Failure and Cardiac Tamponade occurring in the Immediate Post-bypass Period:

- In both conditions, there is increased filling pressure, systemic hypotension, and low cardiac output.
- The classic teaching of equalization of cardiac pressure seen in cardiac tamponade may not be present because areas of focal compression by clotting can markedly decrease the filling of only one chamber.

• **Echocardiography** can be used in diagnosis. The trans-esophageal approach is better than the trans-thoracic approach because the usual trans-thoracic windows may be obscured by dressings and draining tubes.
When the diagnosis is not clear, **surgical re-exploration** may be indicated.

Q: What are the causes of hypotension when the patient is weaned from CPB?
A: Assess the pressure transducer at first. Then search for other causes as above (group II, III, IV).

Treatment of Pump Failure (Group III):

1- Reinstitute CPB.

2- Inotropic Therapy: such as

• **Dopamine:** It is the most commonly used
Advantage: It increases renal blood flow and increases blood pressure > cardiac output.
Disadvantage: It increases the filling pressure, and produces tachycardia and vasoconstriction in high doses, which increase the infarction.
Therefore, most clinicians avoid using inotropes routinely (only when indicated).

• **$CaCl_2$:** 0.5-1.0 gm i.v. bolus (the simplest).
Disadvantage: ▫ It exacerbates myocardial ischemia by causing **coronary vasospasm**.
▫ It exacerbates **reperfusion injury** by causing accumulation of intracellular Ca^{++}.
Therefore, its use should be guided by determination of ionized Ca^{++} level, which should be low, especially in patients who were on Ca^{++} channel blockers preoperatively.

• **Dobutamine**:
Advantage: It does not increase the filling pressure and produces less tachycardia.
Disadvantage: It increases cardiac output without significant increase in arterial blood pressure.

• **Amrinone** (0.75-1.5 mg/kg then 5-10 µg/kg/min i.v. drip),
Milrinone (0.05 mg/kg then 0.5-0.7 µg/kg/min i.v. drip), or
Enoximone
Both are selective phosphodiesterase inhibitors. They have an inotropic and inodilator action (arterial and venous).
Advantages:
▫ They decrease the afterload and do not increase the heart rate; therefore, they decrease myocardial O_2 consumption.
▫ Combination of inodilator and β agonist actions causes a synergistic inotropic effect.

• **Epinephrine:** (0.05-0.2 µg/kg/min by i.v. infusion) It is the **most potent** inotrope.
Advantage: It increases cardiac output and arterial blood pressure.
Disadvantage: Vasoconstriction and tachycardia increase myocardial infarction.

• **Glucose-Insulin-K (GIK) infusion:** It is under research.

• **Thyroid hormone (T_3):** It is under research.

3- Vasodilators: such as nitroprusside or inodilator (as above). They are used to decrease the systemic vascular resistance (if high).

4- Detection of Unrecognized Causes of Pump Failure:
Possible causes can be recognized by **TEE.**
For example: Myocardial ischemia due to a kinked graft or coronary vasospasm.
Valvular dysfunction.
Shunting.
Right ventricular failure (the distention is primarily right sided).

5- Circulatory Assist Devices:
Aim: To assist and provide a circulatory support to:
- Rest a diseased heart.
- Decrease myocardial O_2 demand.
- Maintain adequate end-organ perfusion/function.
- Provide a bridge to heart transplantation.

They include:
- Intra-aortic balloon counter-pulsation (IABCP).
- Temporary implantable ventricular assist devices (VAD)
- Cardiac restraint devices.
- Impella.

a- Intra-Aortic Balloon Counter-pulsation (IABCP):

IABCP was first introduced in 1968. The term "counter-pulsation" is a misnomer for the process of providing pulsatile flow during diastole.

Description:

It is a 90-cm stiff plastic catheter with a 25-cm long large sausage-shaped polyurethrane balloon at its tip, which has a capacity of 40-60 mL (figure 25-14).

Indications:

In general, IABCP is indicated when **cardiac pump failure is life threatening** and either pump function is expected to improve spontaneously or a correcting procedure is planned i.e., it provides **temporary circulatory support**.

1- **IABCP may be used after CBP** if the inotropes and afterload reduction fail and before another attempt is made to wean the patient.

2- Other Indications:

- **Ischemic Heart Diseases:**
  - **Acute myocardial infarction** complicated by:
    - Mechanical defects e.g., ventricular or septal rupture, acute mitral regurgitation, or ventricular aneurysm.
    - Continued ischemic pain and extension of infarction.
    - Unstable angina.
    - Refractory ventricular arrhythmias.
  - **During cardiac catheterization.**
  - **Undergoing non-cardiac surgery.**
  - **Failed Percutaneous Transluminal Coronary Angioplasty (PTCA) and awaiting CABG.**
- **Cardiac Surgery:** ▫ **Before CPB and postoperatively.**
  ▫ **Planned cardiac transplantation.**
- **Pulsatile CPB**, rare.
- **Pediatric congenital heart diseases.**
- **Neurosurgery:** It temporarily increases CBF.

All these indications are expected to resolve.

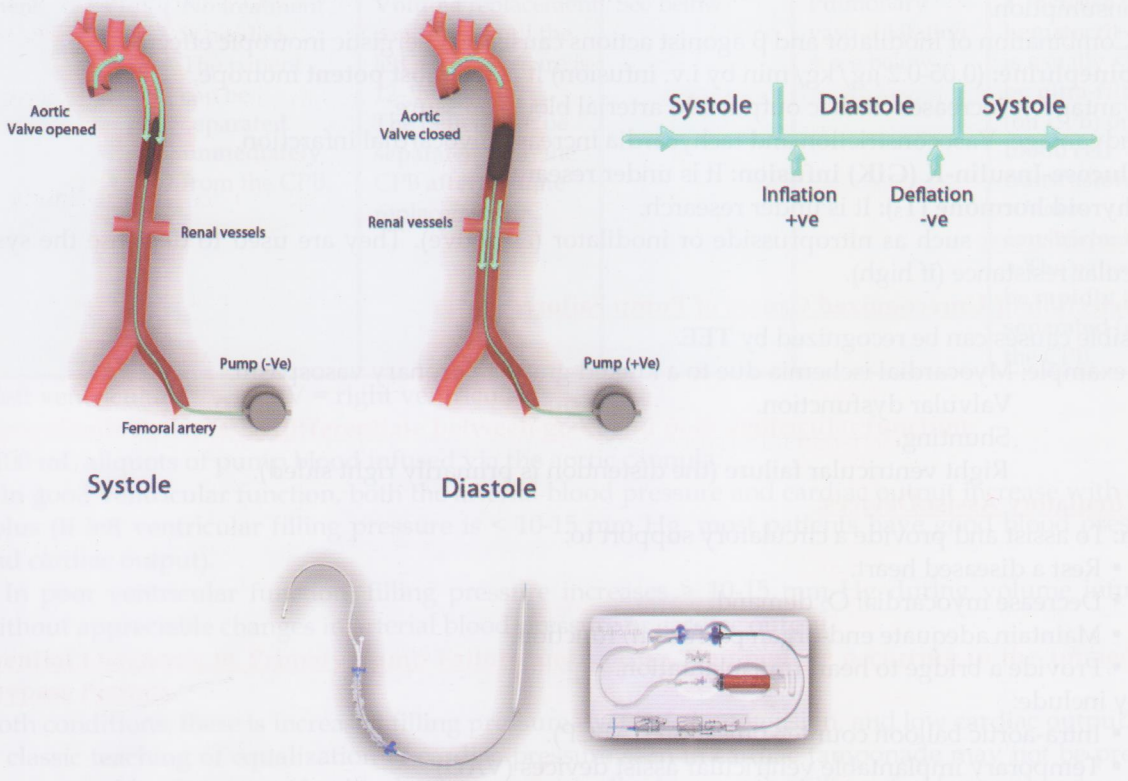


Figure 25-14: IABCP

Technique:

• It is introduced through the **femoral artery** by percutaneous **Seldinger catheterization** (± an introducer sheath that provides a rapid, safe technique with minimal arterial trauma and bleeding) and **positioned in the thoracic aorta** just **distal to the origin of the left subclavian artery** and the balloon end rests **proximal to the origin of renal vessels**. The balloon is available in various lengths to match body height. Correct balloon placement does not require fluoroscopy, which allows for timely placement of the device at the bedside. Other practitioners may check the balloon position on a **chest x-ray** to ensure that the radio-opaque tip is at the level of the second intercostal space (figure 25-15).

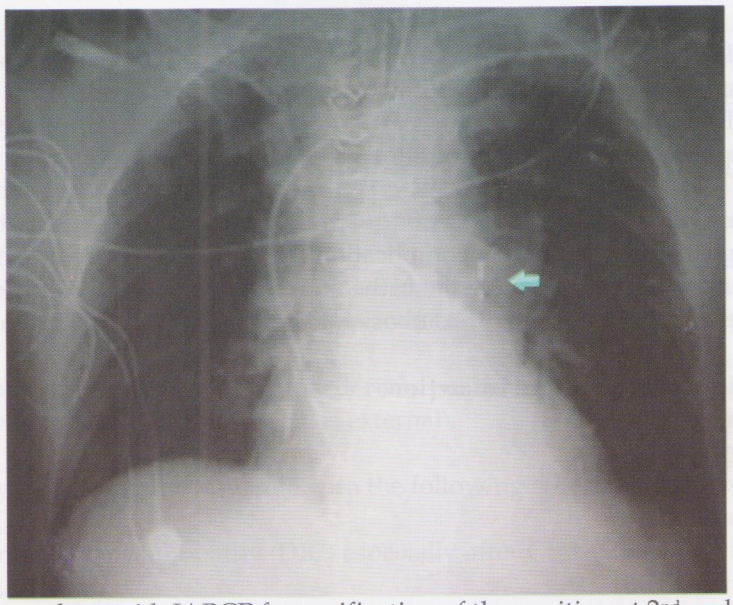


Figure 25-15: Plain x-ray chest with IABCP for verification of the position at 2nd and 3rd intercostal spaces

• Its efficacy is dependent on the proper timing of inflation and deflation.

• The balloon is **best inflated by helium** (its low density facilitates rapid transfer from pump to balloon) **or CO_2 gas just after the dicrotic notch**, after aortic valve closure i.e., **immediately after systole**, with the onset of diastole. This causes **diastolic augmentation** which:

  ▫ augments the diastolic blood pressure by a retrograde flow towards the aortic valve that increases the coronary blood flow.

  ▫ displaces blood from the aorta that increases the peripheral blood flow.

• The balloon is best deflated maximally just before left ventricular ejection i.e., **immediately before systole,** at the end of diastole. This:

  ▫ decreases the afterload by creating low pressure in the aorta (vacuum).

  ▫ augments the cardiac output by 500-800 mL/min and increases contractility (figure 25-16).

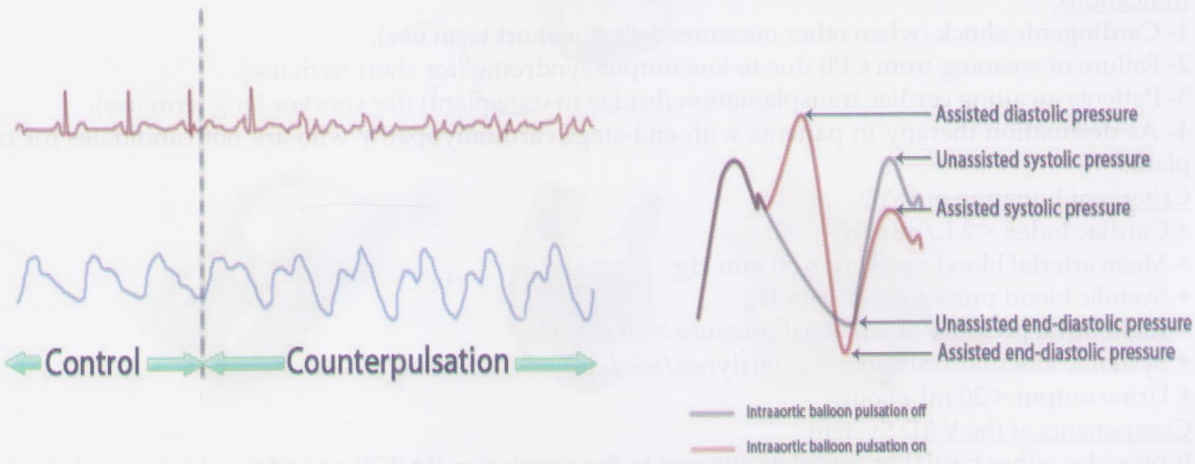


Figure 25-16: Arterial waveform of IABCP

• Anticoagulation: The presence of a large foreign body in the aorta requires **systemic anticoagulation** to prevent thrombosis. The balloon should not be left deflated for longer than a minute while in situ; otherwise, thrombosis may develop despite anticoagulation.
• IABCP is used in a **frequency** of 1: 1 to provide maximal support and the ratio is reduced to 1: 2 then 1: 3 during weaning (i.e., it is inflated and deflated every 3 intrinsic cardiac cycles).
• IABCP is triggered by one of the following methods:
  ▫ The R wave on the ECG,
  ▫ The ventricular pacemaker spike on the ECG, or
  ▫ The upslope of the arterial pressure waveform.

It is set at a preset rate.

Criteria of Weaning:

• Stable heart rate and rhythm.
• Mean arterial blood pressure > 65 mm Hg with little or no vasopressor support.
• Cardiac index > 2.5 L/min/m^2.
• Urine output is adequate.

Complications:

• **Due to decreased cardiac output:**
  ▫ **Ischemia of the leg** is the most common complication (25% of cases), which can involve the ipsilateral or contralateral leg and can appear while the catheter is in place or within hours after the catheter is removed. Most cases are due to *in-situ* thrombosis at the catheter insertion site and require surgical thrombectomy.
  ▫ **Splenic, mesenteric, and spinal cord infarction**.
• **Due to placement:**
  ▫ Dissection of the aorta.
  ▫ Pseudo-aneurysm.
  ▫ Renal artery occlusion.
  ▫ Internal mammary occlusion.
  ▫ Inability to place the IABCP.
• **Due to catheter material:**
  ▫ Thrombus formation and embolization.
  ▫ Thrombocytopenia.
  ▫ Infection.
  ▫ Gas embolization.

Contraindications:

1- Aortic insufficiency.
2- Severe aortic disease e.g., atheromatous, aneurysmal, dissection, but still some use it in these conditions.
3- Renal insufficiency.
4- A recently-placed (within 12 months) prosthetic graft in the aortic aorta.

b- Temporary Implantable Ventricular Assist Devices (VAD):

It can be used as a **temporary or permanent** therapy.

Indications:

1- **Cardiogenic shock** (when other measures fail) (for **short term use).**
2- Failure of weaning from CPB due to low output syndrome (for short term use).
3- Patients awaiting cardiac transplantation (bridge to transplant) (for short or long term use).
4- As destination therapy in patients with end-stage cardiomyopathy who are not candidates for transplant.

Criteria of Initiation of VAD:

• Cardiac index < 2 L/min/m^2.
• Mean arterial blood pressure < 60 mm Hg.
• Systolic blood pressure < 90 mm Hg.
• Right atrial pressure or left atrial pressure > 20 mm Hg.
• Systemic vascular resistance > 2100 dynes/sec/cm^5.
• Urine output < 20 mL/hour.

Components of the VAD System:

It provides either partial or complete support to the circulation (IABCP provides only augmentation of an existing cardiac output).

a- Partial Support: is provided by • right ventricular assist device (RVAD), or
• left ventricular assist device (LVAD).

b- Complete Support: is provided by both RVAD and LVAD (i.e., bi-ventricular assisting device, BiVAD).

The VAD system consists of (figure 25-17 and 25-18):

1. **Cannulas**: They are inserted in:
   - The **right atrium** (as the inflow to the pump) and **pulmonary artery** (as the outflow from the pump), if **RVAD** is needed for short term (temporary) use i.e., when recovery is anticipated.
   - **The left atrium** (as the inflow) and **the aorta** (as the outflow), if **LVAD** is needed for short term use.

   Or • The **apex** of the ventricle (as the inflow), if long term use is needed as **a bridge to cardiac transplant**.
2. **Blood Pumps:** They have either:
   - **A Continuous Flow:** It is used for short term use e.g., post-CPB or a bridge for transplant. It is generated by roller pumps or centrifugal pumps

N.B.: IABCP may be used as an adjunct during continuous flow to provide some pulsatile flow to facilitate cardiac surgery.

- **A Pulsatile Flow:** It is used for long term support e.g., a bridge to transport; so, it needs anti-coagulant therapy. It is generated by:
  - i- Pneumatic Pumps: where air sacs surround a blood sac. The air sacs create negative pressure to facilitate filling and compression of the blood sac ejecting the blood (its pump and console "motor" are external).
  - ii- Electronic Pumps: Their console (motor) derives pusher plates which compress a sac to eject the blood (its pump is internal but the console is external).

Weaning:

It is done gradually by decreasing the flow rate with the following criteria of weaning of the IABCP.

Complications of VAD:

1- Bleeding and disseminated coagulopathy (DIC) especially after CBP, preexisting liver, or renal disease, or the use of anticoagulant.

2- Thrombo-embolic complications as central nervous system deficits; so, anticoagulants are needed.

3- VAD malfunction as an obstruction or tube kink, decreasing the flow rate.

4- Infections, which may lead to multiple organ dysfunction syndrome (MODS).

5- Right ventricular failure and aortic regurgitation in patients with LVAD; therefore, trans-esophageal echocardiography is mandatory.

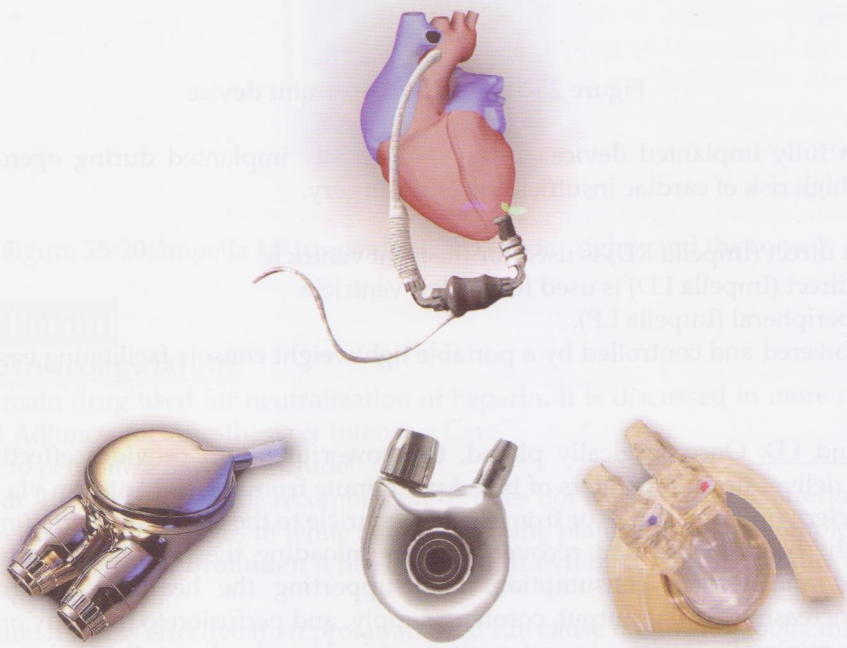


Figure 25-17: VAD connected to the heart (above) and 3 different VADs (below)



Figure 25-18: a console for IABCP or VAD

c- Cardiac Restraint Devices:

They functionally act as a sock placed over the heart to limit its further expansion or even to gradually shrink it. They are inserted via a limited left thoracotomy or by video-assisted thoracotomy (figure 25-19).

Indication:

Patients with advanced congestive heart failure.

Types: There are two types:

- Corcap cardiac support device
- Paracor.

They allow fast-track anesthesia with shorter intensive care and hospital stay.

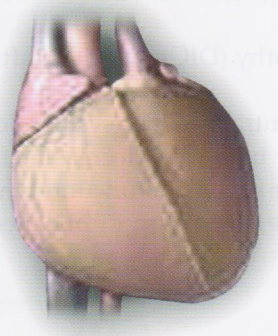


Figure 25-19: A cardiac restraint device

d- Impella:

The Impella is a fully implanted device, which is surgically implanted during open-heart procedures where there is a high risk of cardiac insufficiency after surgery.

Types:

- Impella right direct (Impella RD) is used for the right ventricle.
- Impella left direct (Impella LD) is used for the left ventricle.
- Impella left peripheral (Impella LP).

The Impella is powered and controlled by a portable lightweight console facilitating easy transport of the patient.

Action:

- Impella RD and LD: Once surgically placed, the powerful pump provides effective hemodynamic support and can deliver up to 5-5.5 liters of blood per minute from the right atrium via the outlet graft to the pulmonary artery (in Impella RD) or from the left ventricle to the ascending aorta (in Impella LD). The Impella allows the heart to rest and recover actively unloading the right/left ventricle, reducing the heart's workload and oxygen consumption, and supporting the heart for **up to 10 days** while simultaneously increasing cardiac output, coronary supply, and perfusion to the body organs.
- Impella LP: is a minimally invasive percutaneous ventricular unloading catheter that allows the heart to rest and recover (as above). It is inserted via the femoral artery over a guide wire (Impella LP2.5) or via a cut down (Impella LP5.0). The catheter is advanced into the left ventricle, and the guide wire is then

removed. It can pump either 2.5 or 5 liters of blood/minutes from the left ventricle to the ascending aorta for **up to 5 days** (figure 25-20).

Indications: They are used as a bridge to the next decision.

- Impella RD and LD are used to temporarily support post-cardiotomy cardiogenic shock (low output syndrome) (failure to wean), and acute myocardial infarction patients with impaired right or left ventricular function e.g., after transplantation or coronary bypass surgery. Combination of right and left devices is used for biventricular support. Impella can also be combined with right or left ventricular assist devices for a long-term management.
- Impella LP is used to support patients during post-cardiotomy period (failure to wean) or high-risk percutaneous coronary intervention (PCI), post-PCI period, acute myocardial infarction, and cardiogenic shock.

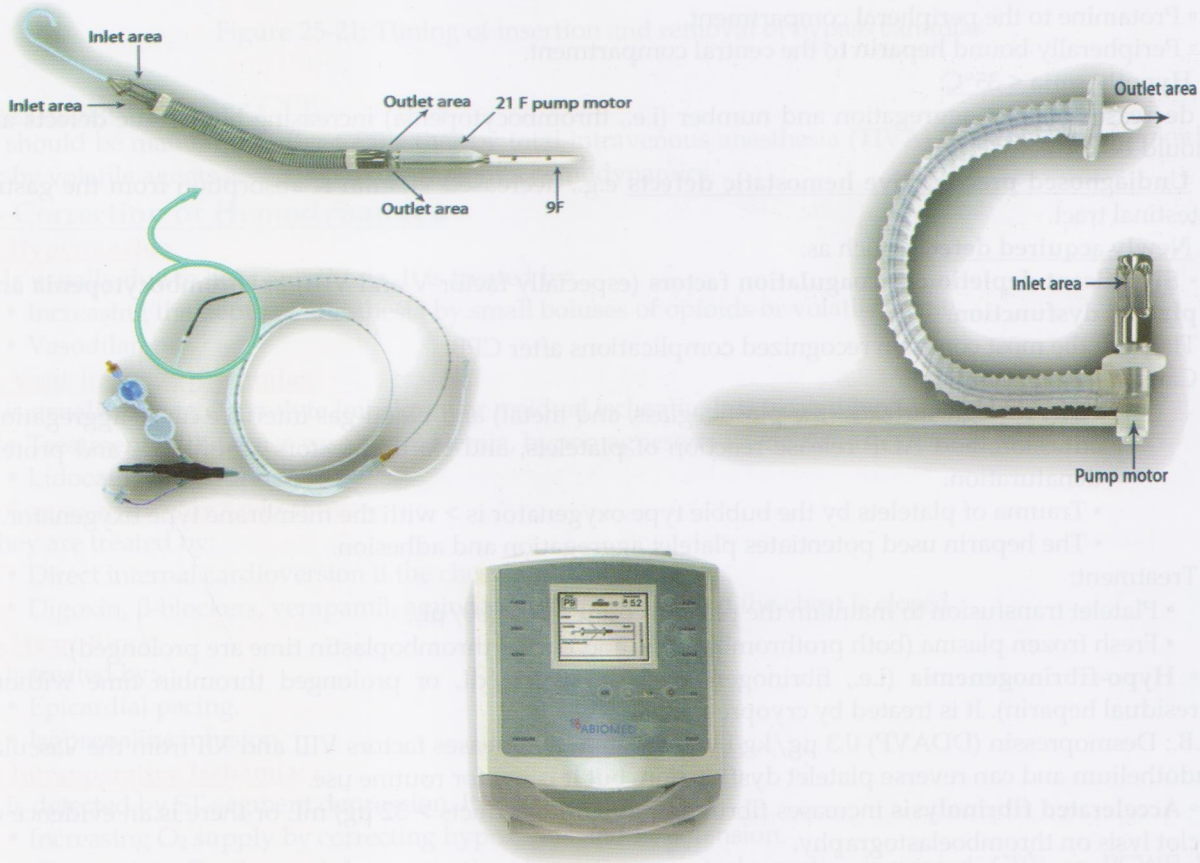


Figure 25-20: Impella LP (upper left), RD (upper right), and the console

Post-Bypass Period

1- Reversal of Anticoagulation:

Protamine is the main drug used for neutralization of heparin. It is discussed in more details in chapter "Pharmacological Adjuncts for Anesthesia & Intensive Care".

Other drugs used to neutralize heparin include:

1- **Platelet Factor 4 (PF4):** (human or recombinant): It does not cause systemic arterial hypotension or pulmonary hypertension or changes in white blood cell count, platelet count, or complement levels.

2- **Polybrene (Hexadimethine Bromide):** It has been withdrawn from clinical use due to nephrotoxicity and pulmonary hypertension.

3- **Toluidine Blue:** It is less effective than protamine and can cause met-hemoglobinemia.

2- Control of Bleeding:

- **Venous cannulas are removed before** the aortic cannula, as the latter can be used as an access allowing rapid administration of a large volume to the patient.

• Most patients need additional blood volume subsequent to the termination of CPB. Administration of blood, colloids, and crystalloid fluids is guided by the filling pressure and post-bypass hematocrit **(a final hematocrit of 25-27% is generally desirable).**

• Blood remaining in the CPB reservoir can be transfused via the aortic cannula (if still in place) or processed by a cell saver device and given intravenously.

• **Causes of Persistent Bleeding and Oozing:** (± clot formation)

1- **Inadequate surgical control of the bleeding sites:** (the most common)

Checking for bleeding especially from **the posterior surface of the heart** requires lifting the heart, which can cause severe hypotension.

2- **Inadequate reversal of heparin:** The ACT should return to the baseline after protamine. Additional protamine (25-50 mg) doses might be needed.

3- **Re-heparinization (heparin rebound):**

It occurs after apparent adequate reversal due to **redistribution** of either:

- Protamine to the peripheral compartment.
- Peripherally bound heparin to the central compartment.

4- **Hypothermia < 35°C**:

It decreases platelet aggregation and number (i.e., thrombocytopenia) increasing hemostatic defects and should be corrected.

5- **Undiagnosed preoperative hemostatic defects** e.g., decreased vitamin K absorption from the gastro-intestinal tract.

6- **Newly acquired defects:** such as:

- **Significant depletion of coagulation factors** (especially factor V and VIII) **or thrombocytopenia and platelet dysfunction:**

  They are the most common recognized complications after CPB.

  Causes:
  - Hemodilution.
  - The foreign surfaces (the plastic, glass, and metal) and blood-gas interface cause aggregation, adhesion, and ADP release reaction of platelets, and clotting factors absorption, and protein denaturation.
  - Trauma of platelets by the bubble type oxygenator is > with the membrane type oxygenator.
  - The heparin used potentiates platelet aggregation and adhesion.

  Treatment:
  - Platelet transfusion to maintain the platelet count > 100 000/µL.
  - Fresh frozen plasma (both prothrombin time and partial thromboplastin time are prolonged).

- **Hypo-fibrinogenemia** (i.e., fibrinogen level < 100 mg/dL or prolonged thrombin time without residual heparin). It is treated by cryoprecipitate.

N.B.: Desmopressin (DDAVP) 0.3 µg/kg i.v. over 20 min increases factors VIII and XII from the vascular endothelium and can reverse platelet dysfunction, but it is not for routine use.

- **Accelerated fibrinolysis** increases fibrin degradation products > 32 µg/mL or there is an evidence of clot lysis on thromboelastography.

  Treatment: Epsilon-amino-caproic acid 4-5 gm followed by 1 gm/h or tranexamic acid 10 mg/kg.

Generally, administration of platelets and coagulation factors should be guided by additional coagulation studies, but empiric therapy may be necessary when such tests are not readily available, as well as after massive transfusion.

• **Recombinant Activated Factor VII:** is used to restore hemostasis that results from severe hemorrhagic complications after CBP. More details are discussed in chapter "Pharmacological Adjuncts for Anesthesia & Intensive Care".

3- Continuation of Patient Re-warming:

After discontinuation of the pump, surface re-warming should continue as heat redistribution may occur resulting in hypothermia (i.e., after drop).

4- Removal of Bypass Cannulas:

The bypass cannulas are removed and the chest is closed. The surgical team should be ready to resume CPB at any time. The timing of insertion and removal of bypass cannulas (arterial and venous) is shown in figure 25-21.

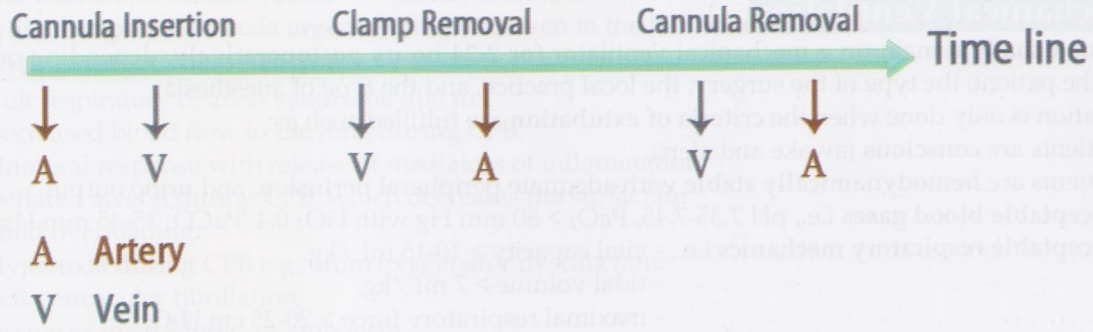


Figure 25-21: Timing of insertion and removal of bypass cannulas

5- Anesthesia after CPB:

It should be maintained after CPB either by total intravenous anesthesia (TIVA) (small doses of opioids) or by volatile agents according to the patient's hemodynamics.

6- Correction of Hemodynamics:

a- Hypertension:

It is usually due to light anesthesia. It is treated by:

- Increasing the depth of anesthesia by small boluses of opioids or volatile agents.
- Vasodilators.

b- Ventricular Arrhythmias:

It is usually due to electrolyte imbalance or residual ischemia. It is treated by:

- Treatment of the cause e.g., hypokalemia, hypomagnesemia…etc.
- Lidocaine or procainamide.

c- Supraventricular Arrhythmias:

They are treated by:

- Direct internal cardioversion if the chest is still opened.
- Digoxin, β-blockers, verapamil, amiodarone, or adenosine if the chest is closed.

d- Heart Block:

It is treated by:

- Epicardial pacing.
- Isoprenaline infusion.

e- Intraoperative Ischemia:

It is detected by ST-segment depression. It is treated by:

- Increasing O_2 supply by correcting hypoxemia and hypotension.
- Decreasing O_2 demand by correcting hypertension, tachycardia, increased CVP or PCWP by deepening anesthesia or by using vasodilators or propranolol.

7- Patient Transportation: (from the operating room to the intensive care unit)

- Before the end of the operation, the following preparations **should be ready**:
  - Portable monitoring equipment; at least ECG, invasive blood pressure, pulse oximetry, ± CVP.
  - Portable infusion pumps.
  - A full O_2 cylinder with a self-inflating bag.
  - An endotracheal tube, laryngoscope, succinylcholine, and emergency resuscitation drugs should also accompany the patient.
- **Sedation** by a small amount of opioid during transfer.
- Upon arrival to the intensive care:
  - The patient should be attached to the ventilator, and breath sounds should be checked.
  - The patient should be attached to monitors and infusions.
  - The intensive care staff should be given a brief summary of the procedure, intraoperative problems, current drug therapy and any expected difficulties.

Postoperative Management and Intensive Care Considerations

1- Mechanical Ventilation

• Patients usually remain on a mechanical ventilator **for 2-24 hours postoperatively,** depending on the type of the patient, the type of the surgery, the local practice, and the type of anesthesia.

• Extubation is only done when the **criteria of extubation** are fulfilled such as:

- Patients are **conscious** (awake and alert).
- Patients are **hemodynamically stable** with adequate peripheral perfusion, and urine output.
- **Acceptable blood gases** i.e., pH 7.35-7.45, PaO_2 > 80 mm Hg with FiO_2 0.4, $PaCO_2$ 35-45 mm Hg.
- **Acceptable respiratory mechanics** i.e., - vital capacity > 10-15 mL/kg.
  - tidal volume > 7 mL/kg.
  - maximal respiratory force > 20-25 cm H_2O.
- **Good muscle power.**
- **Hemostasis** i.e., < 200 mL/h chest tube drainage.
- **Stable metabolic state** i.e., normal temperature and electrolytes.

• **Most patients** are **extubated by the following morning** and are put on continuous positive airway pressure (CPAP) of 5 cm H_2O with 50% O_2. If the patient tolerates this CPAP for 30 min with acceptable arterial blood gases, the patient is extubated.

• **Some centers** do **early extubation on the operating table or within 2 hours of surgery**. This is called fast tracking provided that the criteria of extubation are met, but this demands changes in the technique as follows:

- Cross clamping and bypass **times** must be **brief.**
- **Intermittent cross clamping with fibrillation** is used (i.e., warm) rather than cold cardioplegia and systemic hypothermia.
- **Active vasodilator therapy during re-warming** is used to decrease the temperature after-drop after CPB.
- Anesthetic techniques include:
  - The use of relatively **small doses of fentanyl** (1.5-15μg/kg), alfentanil, sufentanil, or remifentanil.
  - **Atracurium or vecuronium** for muscle relaxation instead of pancuronium.
  - **Inhalational agents as isoflurane or sevoflurane or i.v. agents as propofol** that are used for maintenance.

2- Close Observation of the Patient

for maintaining hemodynamic stability and detecting postoperative complications.

3- Fluid Therapy

It should be **guided by filling pressures**. Most patients require a good volume for several hours after surgery.

4- Postoperative Analgesia

According to the anesthetic technique, timing of postoperative analgesia is determined by:

• I.v. opioids either bolus or infusion.

• Propofol infusion 1-2 mg/kg/h.

• **Regional techniques are not popular because coagulation defects** are common, but prebypass intrathecal opioid with postoperative epidural block has been reported. **Thoracic epidurals** are used in some centers, claiming improved hemodynamic stability and excellent postoperative pain relief, but this is controversial due to the perceived risk of epidural hematoma and tetraplegia following anticoagulation.

5- Postoperative Complications (= Complications of CPB)

1- Cardiovascular Complications:

• Congestive heart failure.

• Arrhythmias.

• Pump failure (low output) syndrome.

• Myocardial ischemia or infarction due to:
- Surgical manipulation.
- Prolonged CPB and aortic cross clamping.
- Use of cardioplegic solutions.
- Occlusion or kinking of grafts.

- Aortic dissection from cannulas or clamps.
- Generalized or localized venous congestion from kinked or misplaced return lines.
- Cardiac tamponade: needs urgent exploration even in the intensive care unit.

2- Pulmonary Complications:

- Adult respiratory distress syndrome due to:
  - Decreased blood flow to the lung during CPB.
  - Humoral response with release of mediators of inflammation.
  - Deflated alveoli during CPB, which decreases the surfactant.
  - Fluid overloading.
  - Hyperoxia during CPB e.g., from oxygenator dysfunction.
  - Left ventricular fibrillation.
- Massive or microscopic air embolism.

3- Renal Complications:

- Polyuria due to hemodilution and diuretics.
- Oliguria due to hypoperfusion.

4- Postoperative Bleeding:

- Causes of postoperative bleeding are discussed above. Close monitoring of chest tube drainage is essential. In the first 2 hours, > 250-300 mL/h is considered excessive.

  After the first 2 hours, > 100-200 mL/h is considered also excessive.
- Immediate sternotomy and exploration are essential.
- Blood transfusion is usually needed if hematocrit becomes <35%.

5- Embolism:

It may occur due to air, destroyed or aggregated formed blood elements, fat, or endogenous debris.

6- Hyperglycemia:

It may occur due to increased catecholamine levels, which inhibit insulin secretion and produce a direct action in the form of catabolism of glycogen into blood glucose.

7- Hypokalemia and Hypomagnesemia:

They may occur due to hemodilution or usage of diuretics intraoperatively.

8- Central Nervous Complications:

- Neurological complications occur in 40%-80% of cases and persist in 30% of patients. They are either:
  - **Transient neuro-psychiatric dysfunction** (the most common) ranging from subtle cognitive and intellectual changes to delirium and organic brain syndromes. Postoperative cognitive dysfunction is discussed in more details in chapter "Anesthesia and Geriatric Patients".
  - **Strokes** (less common) that occur in 2-5% of cases.
- Factors increasing neurological complications include:
  - Intra-cardiac (valvular) procedures.
  - Advanced age.
  - Preexisting cerebro-vascular diseases.
  - Aortic atheroma.

Prophylaxis against strokes (Cerebral protection) during CPB (see above).

6- Anti-Platelet Therapy

Antiplatelet therapy is administered to prevent thrombus formation in cardiac surgery such as abciximab, eptifibatide, tirofiban, or clopidogrel. These drugs are discussed in more details in chapter "Pharmacological Adjuncts for Anesthesia & Intensive Care".

Q: What are the different hematological aspects of cardiac surgery?

A: They include:

1- Bleeding prophylaxis.

2- Anticoagulation (in addition to ACT and heparin-dose response curve).

3- Reversal of anticoagulation.

4- Causes of persistent bleeding and oozing after CPB (and its management such as activated factor VII).

5- Anti-platelet therapy.

All these aspects are discussed above.

Q: What are the emergencies after cardiac surgery?

A:
- *Weaning of the bypass; hypovolemic, pump failure, and hyperdynamic status.*
- *Postoperative complications.*

Redo Coronary Arterial Bypass Graft

The number of redo coronary arterial bypass grafts increases nowadays due to:

- Increased number of cardiac surgeries.
- Increased number of patients who live longer after cardiac surgeries. They develop new pathological changes requiring surgical interventions.

Third, fourth, and even fifth reopen have been reported.

Anesthetic Management and Considerations

The same as anesthetic management as cardiac surgery wit the following considerations:

Preoperative Management and Consideration

- There is often **poor left ventricular function**.
- **Venous/arterial access** as for CABG, but often **more difficult**.
- **Patients on anti-platelets** which should be stopped for one week-10 days if possible; otherwise aprotinin, fresh frozen plasma, platelets should be given.
- **Cross-matched six units of blood** should be available in the theater before the start of surgery.
- Risk factors include:
  - Increased age.
  - Advanced disease.
  - Impaired cardiac function.
  - Pre-existing ischemia.
  - Acute hemodynamic instability.

Intraoperative Management and Considerations

- Difficult surgical dissection is common with **possibility of catastrophic hemorrhage**.
- **Prolonged anesthesia, surgery, and bypass times**.
- **Hemodynamic instability** is common. Ventricular support by pharmacological or mechanical means is usually needed.
- **Surgical incisions can be variable** such as thoracotomy rather than mid-thoracotomy.
- **Femoral artery** is usually used **for cannulation**.
- A **pulmonary arterial flotation catheter introducer or a rapid infusion device** is useful if rapid infusion is necessary.
- Have **external defibrillator pads *in situ* on the patient**, as ventricular fibrillation is a risk at sternotomy and dissection of adhesions. This can be a problem with the use of diathermy as it obscures the ECG, but ventricular fibrillation should be suspected if a flat arterial trace is seen.
- There is a **risk of torrential bleeding** as the right ventricle may be stuck by adhesions to the underside of the sternum.
- Consider using **a fibrinolytic inhibitor such as aprotinin** during the procedure.
- Consider using **trans-esophageal echocardiography and cell savers**.
- Consider using **off-pump surgery** if possible with readiness for exploration

Postoperative Management and Considerations

- There is increased **risk of postoperative bleeding**, which may need immediate exploration.
- There may be problems related to **poor left ventricular function**, which needs support.
- Prolonged **intensive care unit stay and postoperative ventilation**, which increase the cost.
- Increased incidence of **postoperative organ dysfunction and failure**.
- Increased incidence of **postoperative** acute ischemia and myocardial infarction.

Emergency Coronary Arterial Bypass Graft (Failed Angioplasty)

This is a true emergency condition due to complications of angioplasty such as rupture coronary artery (resulting in acute cardiac tamponade) or acute obstruction of coronary artery (resulting in acute myocardial infarction), which necessitate urgent CABG.

In addition to the usual anesthetic management of cardiac surgery, the following considerations should be maintained.

Preoperative Considerations

- The patient is **collapsed and shocked (i.e., peri-arrest)** with the need for urgent surgery to relieve tamponade and to correct ischemia.
- The patient **usually has good femoral and arterial access** from the 'cath lab'.
- The patient should have **hemodynamically stable status by inotropes**; otherwise, cardiac arrest will occur after induction of anesthesia. **Intra-aortic balloon counter-pulsation device** may be needed.

Intraoperative Considerations

- A **pulmonary arterial flotation catheter** may be needed (in addition to the previous monitors), but it may waste time.
- **Very smooth induction** is essential with a reduced dose of fentanyl and etomidate to maintain cardiovascular stability.
- Adrenaline should be prepared to be given as a bolus, 10 or 100 µg/mL as necessary.
- Institute CPB as soon as possible.

Postoperative Considerations

- **Hemodynamic stability should be maintained** postoperatively with inotropes and/or an intra-aortic balloon counter-pulsation device.
- **Delayed extubation** is usually required to help in maintaining hemodynamic stability.
- There is a high risk of **renal failure**.

Anesthetic Management of Cardiac Surgery in Pediatric Patients

Preoperative Management

Preoperative Assessment:

1- Cardiovascular Assessment:

- The **preoperative cardiovascular assessment of patients** with a congenital heart disease is discussed in more details in chapter "Congenital Cardiovascular Disease".
- In **patients with ductal-dependent lesions, prostaglandin E_1 infusion** (0.05-0.1 mg/kg/min) may be used preoperatively to prevent closure of the ductus arteriosus for survival.
- **Manage possible complications** such as congestive heart failure.

2- Assessment of Other Systems and Other Congenital Anomalies.

Preoperative Preparation:

1- Preoperative fasting is maintained as usual. It is discussed in more detains in the chapter of "Pediatric Disease". **Preoperative i.v. infusion** is given to maintain fluid requirements especially for

- patients susceptible to dehydration,
- patients with severe polycythemia, and
- cases with prolonged fasting.

2- Adjust acid-base and electrolyte disturbances and parenteral nutrition to help in recovery of myocardial, renal, and hepatic function.

3- Premedications:

a- Sedatives: Sedatives are essential for **older patients (older than infants)** especially those **with cyanotic lesions** e.g., Fallot tetralogy, because agitation and crying increase the right to left shunting. For example:

- Midazolam 0.5-0.6 mg/kg orally, 0.2 -0.3 mg/kg intra-nasally, or 0.08 mg/kg i.m.
- Morphine 0.1 mg/kg i.m. with pentobarbital 2-3 mg/kg i.m.

I.m. injection itself can increase crying and agitation of the child; therefore, oral or intranasal route is more preferred.

b- Anticholinergics: They are needed for all patients to counteract the enhanced vagal tone; for example, atropine 0.02 mg/kg (minimum dose 0.15 mg) i.m.

Intraoperative Management

Anesthetic Aim:

Anesthetic aims **differ according to the type of the congenital cardiovascular disease**; obstructive lesions, left-to-right shunts, right-to-left shunts, separation or mixing of the pulmonary and systemic circulation. They are discussed in the chapter of "Congenital Cardiovascular Diseases".

Venous Access

- It is desirable, but not always necessary for induction.
- **Avoid agitation and crying** on establishing a venous access especially in patients **with cyanotic lesions** as they increase the right to left shunting. Therefore,
  - Use **EMLA cream** to facilitate cannulation before induction.
  - **Cannulate after induction but before intubation.**
- I.v. fluids, typically at least 2 i.v. fluid infusions are required, one of them in the central venous catheter.
- Extreme caution is necessary to **avoid even the smallest air bubbles**, to avoid paradoxical air embolism via shunt lesions of any direction or patent foramen ovale. Aspiration before each injection prevents dislodgement of any trapped air at the injection port.

Monitoring:

Before Induction

- **Standard monitors** such as ECG, pulse oximeter, non-invasive blood pressure, and end-tidal CO_2 are required.
- A large discrepancy between end-tidal CO_2 and $PaCO_2$ should be anticipated in patients with large right- to-left shunts because of the increased dead space.

After Induction

1- Invasive Arterial Blood Pressure:

It is performed by using a 20-22 gauge cannulas (24 gauge cannula in smaller neonates and prematures) in the radial artery. A cut down may be needed in some instances.

2- Central Venous Pressure:

The internal or external jugular veins are commonly used. If unsuccessful, it may be placed intra-operatively by the surgeon.

3- Pulmonary Artery Catheter:

It is less commonly used. 7 F catheter is used for patients > 25 kg body weight.
5 F catheter is used for patients 7-25 kg body weight.

4- Trans-esophageal Echocardiography:

It is extremely valuable in pediatric patients especially for assessing surgical repair after CPB.
It is most useful in **patients > 12 kg** because the probes required for smaller patients have less resolution.
Epicardial echocardiography is commonly used either in addition to or instead of trans-esophageal echocardiography.

Induction:

a- In Premature Infants and Young Neonates:

Awake intubation is done after adequate preoxygenation.

b- In Older Children: either;

1- I.v. Induction:

For example, thiopental 3-5 mg/kg,
ketamine 1-2 mg/kg,
fentanyl 25-50 µg/kg or sufentanil 5-15 µg/kg for critically ill patients when postoperative ventilation is planned.

The onset of i.v. agents is more rapid in patients with a right to left shunt. All drugs should be given slowly to avoid transiently high arterial blood levels, but the onset is delayed in patients with left to right shunts because circulation dilutes the arterial blood concentration.

2- I.m. Induction:

For example, ketamine 4-10 mg/kg. Its onset of action is 5 min. It is the drug of choice in:

- agitated and uncooperative patients,
- patients with poor cardiac reserve,
- patients without venous access, or
- patients with cyanotic lesions because it does not increase the pulmonary vascular resistance in children.

3- Inhalational Induction:

- For example, halothane or sevoflurane; they are the drugs of choice in:
  - patients with cyanotic lesions as they cause minimal systemic vasodilation,
  - patients with good cardiac reserve. Inhalational agents should not be used in patients with poor cardiac reserve because they cause myocardial depression.

• The same technique as in non-cardiac surgery, but more slowly increase the concentration, to avoid excessive myocardial depression.
• N_2O is usually used with the inhalational agent in a concentration not more than 50% especially in cyanotic lesions (N_2O does not increase pulmonary vascular resistance in pediatric patients).
• The uptake of inhalational agents especially the less soluble agents such as N_2O may be slowed in patients with right to left shunts, in contrast, no significant effect on the uptake is generally observed with left to right shunts.

Intubation:

It is facilitated by either: • Pancuronium 0.1 mg/kg (which is useful due to its vagolytic effect) or
• Succinylcholine 1.5-2.0 mg/kg (less common).

Maintenance:

a- Patients with Good Ventricular Function:

Inhalational agents and N_2O are commonly used.
• Isoflurane is preferred as it causes less myocardial depression and less bradycardia.
• **N_2O** may cause **myocardial depression** in patients with poor cardiac reserve. It should be **stopped in all patients before CPB** to decrease the incidence of intravascular air bubble expansion.

b- Patients with Poor Ventricular Function:

An opioid such as fentanyl or sufentanil is used.

Cardio-Pulmonary Bypass

The same anesthetic management and considerations as that of adults except:
1- **Blood is used to prime the machine** for neonates and infants to prevent excessive hemodilution, because the smallest circuit volume used is still about 700 mL; so, if 700 mL fluid is used, severe hemodilution occurs.
2- **Steroids as methylprednisolone or dexamethasone** may be administered in the by-pass period to attenuate the inflammatory response and ischemia-reperfusion injury in neonates and children.
3- **Dose of heparin before CPB in children:**
• For patients less than 30 kg, 200 IU/kg is given.
For patients more than 30 kg, 300 IU/kg is given.
• The large circuit prime volume to blood volume ratio would be expected to **decrease plasma heparin levels with initiation of CPB** unless an appropriate quantity of heparin is added to the CPB prime.
• Most institutions add heparin to the CPB prime as follows:
▫ Patients less than 30 kg, 2.5 IU/mL of CPB prime
▫ Patients more than 30 kg, 3.0 IU/mL of CPB prime.
• Heparin should always be given **into a central line** through which venous return can be demonstrated easily or **more commonly in infants/neonates directly into the heart** (usually the right atrium) by the surgeon. This is necessary to ensure that heparin dose has reached the central circulation.
4- **CPB** may be complicated by **decreased mean arterial blood pressure, which decreases the systemic perfusion** due to ▫ presence of intra- and extra-cardiac shunts, or
▫ very compliant arterial system in very young patients.
Therefore, • **Shunts** should be controlled as much as possible at the start of the bypass.
• **High flow rates** (up to 200 mL/kg/min) should be used to ensure adequate perfusion in very young patients.
5- **Surgical correction of complex congenital lesions** may need complete circulatory arrest under deep profound hypothermia **(hypothermic circulatory arrest)**. With a 15°C core temperature, circulatory arrest up to 60 min is safe.
Brain protection is usually needed; by ice packing around the head, methyl-prednisolone 30 mg/kg, mannitol 0.5 gm/kg, and phenytoin 10 mg/kg.
6- **Cardioplegia: Cold crystalloid or blood cardioplegia** can be used. **Retrograde cardioplegia or hot shot cardioplegia** can be also used.
7- **Weaning from CPB:**
It is **usually easy** and **primary pump failure** is unusual. **Management of difficult weaning (if occurs)** is as that of adult.
8- **Hemostatic defects:**
They are common in the post-bypass period due to the large priming volumes used (often 200-300% of patient's blood volume) leading to dilution of clotting factors and platelets.

Treatment: ▫ Heparin reversal.
▫ Fresh frozen plasma and platelets.
▫ The use of fresh whole blood transfusions instead of packed red blood cells, which decreases the need for platelets and clotting factors.

9- **Extubation:**

It is only done for: ▫ older children > 6 months,
▫ relatively healthy patients,
▫ patients undergoing simple procedures e.g., closure of a small patent ductus, atrial septal defect, or repair of aortic coarctation.

Differences in CPB between Adults and Children:

CPB	Adults	Children
Perfusion pressure (MAP) (mmHg)	50-80	**30-40**
Flow rates (mL/kg/min) at normothermia	50-70	**100-150**
Hemodilution	+	**++++** (if the priming fluid is not blood).
Temperature	28-32	**15-20** in some cases
Venous drainage problems	Rare	Common
Aortic cannula obstructing aortic outflow	Not a problem	Common due to the small aortic lumen
Cannula placement technically	Easier	More difficult

New Aspects for Myocardial Revascularization

Recently, several new aspects, techniques, and modifications are applied. The recent techniques discussed above include:

1- Tepid cardioplegia and hot shot cardioplegia.
2- Ventricular assist devices.
3- Cardiac restraint devices.
4- Impella.
5- Fast-track extubation.

Other recent techniques include:

1- Off-pump coronary artery by-pass grafting (OPCAB) (Beating heart surgery).
2- Intermittent cross clamping and fibrillation technique.
3- Alternative surgical approaches to full sternotomy.
4- Port access cardiac surgery.
5- Miniature axial flow pumps.
6- Arterial conduits.
7- Reperfusion injury
8- Ischemic preconditioning.
9- Surgical ventricular restoration or Dor procedure.
10- Trans-myocardial laser revascularization and stem cell therapy.

1- Off-Pump Coronary Artery Bypass Grafting (OPCAB) (Beating Heart Surgery)

Coronary artery grafting **on a beating heart** has been first described in the 1960s. It has the following advantages:

- Avoiding many complications of CPB e.g., central nervous sequelae, arrhythmias…etc.
- Decreasing the need for blood transfusion.
- Decreasing the cost.

Anesthetic Management:

Anesthetic management is the same as ordinary CABG, in addition to the following considerations:

1- Inducing Bradycardia:

- Because the slower the heart, the easier it would be for the surgeon.
- The drugs that slow the heart are controversial because they depress the cardiac function, but they decrease the heart rate resulting in a decrease in the O_2 need and protection against ischemia; for example, β-blockers or Ca^{++} channel blockers (avoid pancuronium use).

• Prophylactic antiarrhythmic therapy such as magnesium, lidocaine, or amiodarone is often administered before off-pump CABG.

2- Epicardial Stabilizing Devices:

• Recently with the widespread use of **epicardial stabilizing devices** e.g., Octopus that immobilize the heart at the site of anastomosis, the need for bradycardia has almost disapproved.

The Octopus epicardial stabilizing device **uses suction to stabilize and lift the anatomic site** rather than compress it down, allowing greater hemodynamic stability (figure 25-22). Nowadays, special epicardial stabilizers are designed to do off-pump, via porto-access techniques.

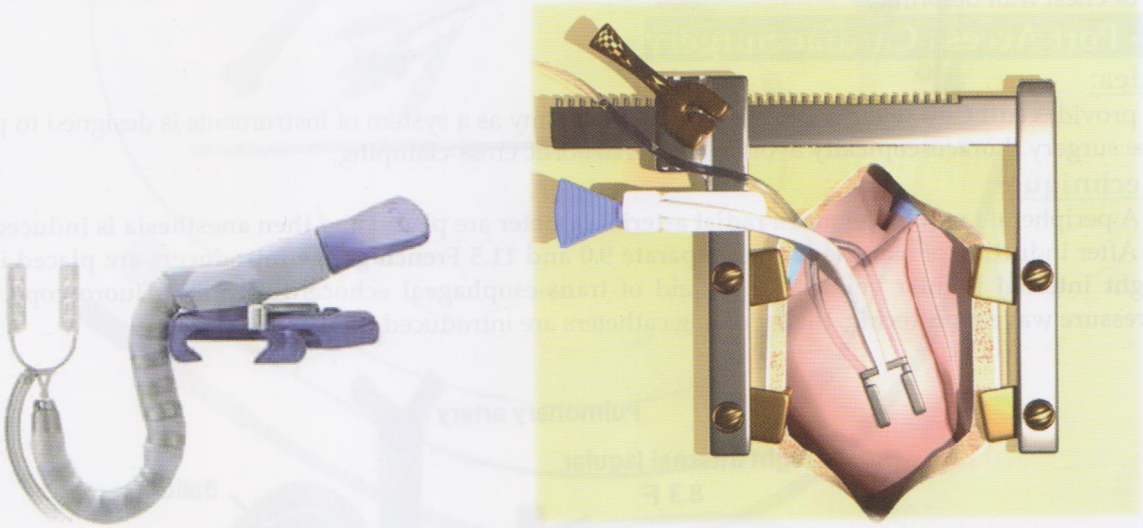


Figure 25-22: Octopus retractor

3- Anticoagulation:

• **Partial anticoagulation (partial heparinization)** is usually needed e.g., 100-150 units heparin/kg **(i.e., 1/2 the dose)** to achieve ACT 250-300 sec (1/2 time), then it is fully reversed with protamine after the grafts are completed.

• Some centers use **full heparinization dose** as that of the traditional CPB.

4- Usage of a Silicon Stent:

The presence of a beating heart makes suture placement for the distal anastomosis difficult. In this regard, a silicon stent can be placed in the target coronary artery during the anastomosis to maintain coronary flow. The silicon stent is removed just before completing the anastomosis.

5- Readiness for CPB:

CPB must be immediately available as surgeons may use CPB if the patient needs.

6- Maintenance of Myocardial Perfusion:

As there is no pump, avoiding tachycardia and maintaining myocardial perfusion is important. These are the tasks of anesthesiologists.

2- Intermittent Cross Clamping and Fibrillation Technique

• This technique is performed during arterial grafts instead of the conventional cardioplegia where the aorta is cross-clamped and a fibrillator pad is placed underneath the heart. When the heart fibrillates, oxygen demand is reduced, and the lower end of a graft can be sutured.

• After each graft, the cross-clamp is removed and the heart is cardioverted into sinus rhythm. The top end will then be sutured onto the aorta. As the heart is not protected by cardioplegia, surgical time needs to be kept to the minimum to avoid myocardial damage.

• Advantages: ▫ No cardioplegia is used (hence a lower incidence of complete heart block).
▫ After applying each graft, the ECG can be inspected for any ischemia.

3- Alternative Surgical Approaches to Full Sternotomy

1- Minimally Invasive Direct Coronary Artery Bypass (MIDCAB):

It is a **small left anterior transverse thoracotomy**, for access of left anterior descending and diagonal arteries (the most popular) by using a left internal mammary artery graft.

2- Right thoracotomy for the access of right coronary artery.

3- A variety of para-sternal or partial sternotomy incisions.

None of these approaches provides an access to all regions of the myocardium. These incisions may require placing supports under the patient's side or back.

N.B.: Full Sternotomy: (the ordinary large incision)

It has many disadvantages such as:

- Resuming normal upper limb activity does not occur before 6-8 weeks.
- It is bad cosmetically.
- It produces more pain.
- It is not suitable in patients with previous sternotomy with an intact internal mammary artery graft, or chest wall deformity.

4- Port Access Cardiac Surgery

Idea:

It provides **full CPB** without the need for a sternotomy as a system of instruments is designed to perform the surgery **thoracoscopically** avoiding external aortic cross-clamping.

Techniques:

- A peripheral **i.v. catheter** and a **radial arterial catheter** are placed and **then anesthesia is induced.**
- After induction of anesthesia, **two separate 9.0 and 11.5 French gauge introducers are placed into the right internal jugular vein.** With the aid of **trans-esophageal echocardiography, fluoroscopy, and/or pressure wave monitoring**, the following catheters are introduced (figure 25-23):

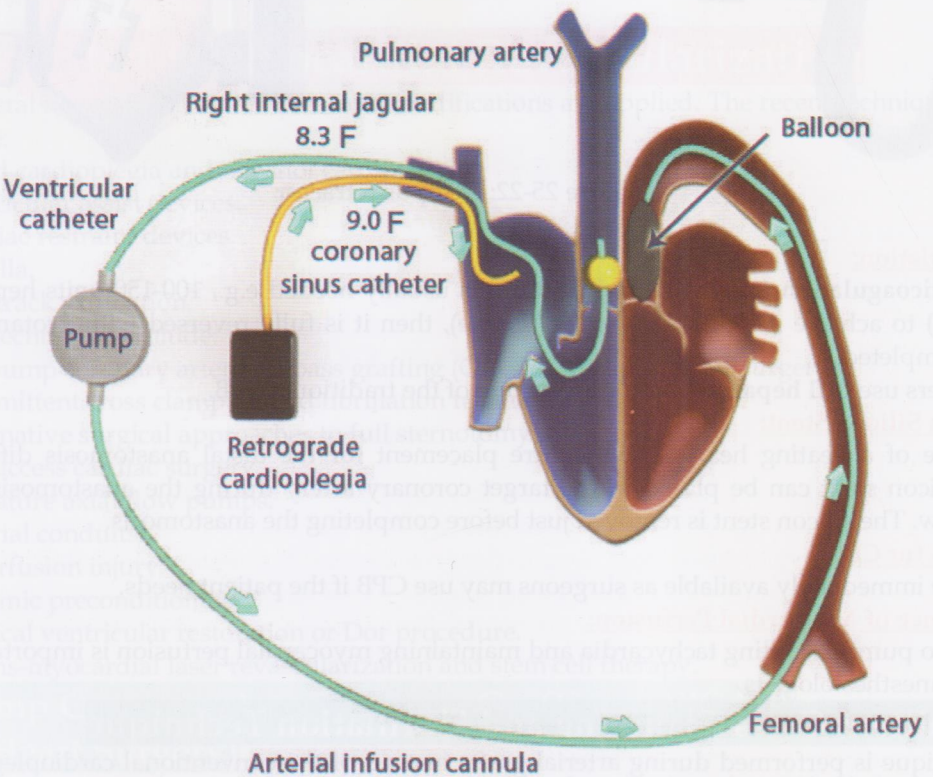


Figure 25-23: Port-access cardiac surgery

- A 9.0 French **coronary sinus catheter** is placed via the larger introducer (11.5) for delivery of **retrograde cardioplegia** later.
- Then a non-balloon tipped 8.3 French **ventricular catheter** is placed via the smaller introducer (9) into the pulmonary artery using a 5 French balloon tipped catheter as a guide **to carry the venous return to the pump.** This catheter can be introduced via the femoral vein (figure 25-24).

- The surgeon then accesses **the femoral artery** for placement of **an arterial infusion cannula** and an endo-aortic balloon occlusion catheter for:
  - aortic occlusion,
  - antegrade cardioplegia infusion, and
  - aortic root venting.

It passes through the femoral arterial cannula into the ascending aorta, just distal to the coronary ostia guided by trans-esophageal echocardiography and fluoroscopy. Nowadays, a modified cannula is placed through a thoracic puncture guided by direct vision via a small thoracotomy incision.

- The CABG procedure is performed with **full CPB and hypothermia.**

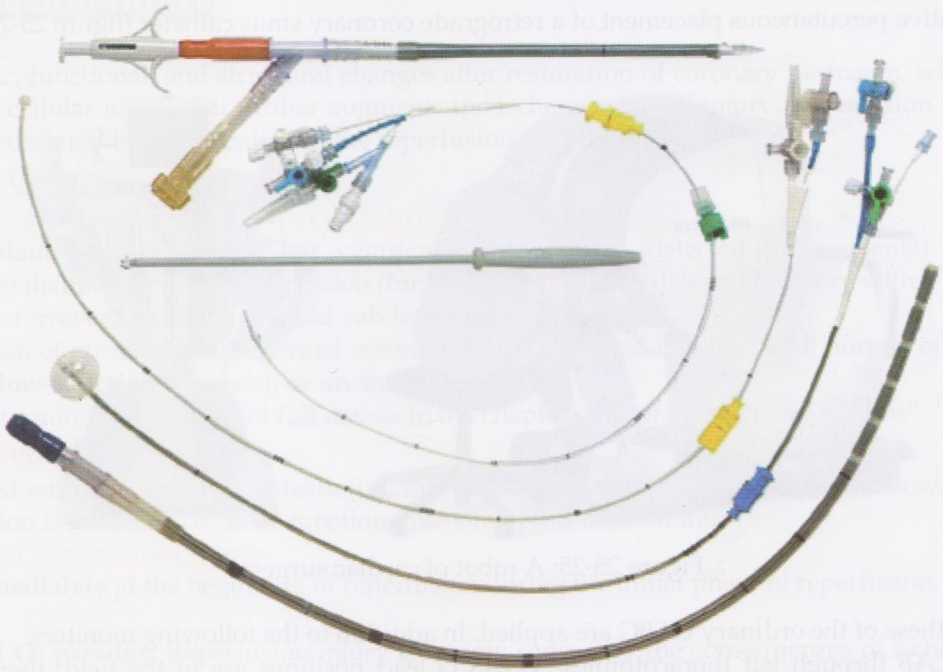


Figure 25-24: A port access cardiac surgery kit

Advantages:

1- **Lower** incidence of **neurological** sequelae.
2- **Less** postoperative **pain.**
3- **Shorter** postoperative intensive care unit and hospital **stay**.

Disadvantages:

1- Added **cost.**
2- **Surgical time** is likely to be **increased.**
3- **No long term results** are available.
4- **Complications of endoaortic balloon** e.g., tendency to migrate, decreased ability to evacuate air, aortic or iliac/femoral dissections.
5- The femoral artery retrograde perfusion technique increases **neurological complications and increases leg ischemia.**

Anesthetic Management:

Anesthetic Techniques:

1- **Fast track management** can be used where the extubation is done within 2 hours either in the operating room or in the intensive care unit (see before).
2- **One-lung ventilation** technique is the most commonly used, if a midline sternotomy incision is not used.
3- **Regional (neuraxial) techniques** can be used such as:
   - **Combined general anesthesia and thoracic epidural anesthesia.**
   - **Thoracic epidural anesthesia alone.**

Care is taken for avoiding the epidural hematoma; therefore,
   - The epidural catheter is placed 12-24 hours preoperatively if CPB is involved or potentially involved.
   - Intrathecal opioids, by a small needle (24 G or smaller), are placed immediately if high heparin dose (CPB) or moderate heparin dose (OPCAB/MIDCAP) is used.

4- **Other regional techniques** can be used for postoperative analgesia such as:
   - Continuous wound infiltration with local anesthesia through multi-orifice catheters.
   - Intercostal nerve cryo-ablation.

- Intra-pleural analgesia.
- Para-vertebral block.
- Para-sternal block.

5- **Robotics:** A robot has recently been used to perform some steps of the surgical procedures such as:
- Distal coronary anastomosis.
- Preoperative percutaneous placement of a retrograde coronary sinus catheter (figure 25-25).



Figure 25-25: A robot of cardiac surgery

Monitoring:

Monitors as these of the ordinary CABG are applied, in addition to the following monitors:
- In MIDCAB through left thoracotomies, V_{4-5} ECG lead positions are in the field; therefore, **sterile needle electrodes are used.**
- **Monitoring the adequacy of cerebral perfusion** (e.g., **trans-cranial Doppler**) is important because malposition of the endoaortic occlusive balloon could threaten the cerebral vessels.
- Trans-esophageal echocardiography is essential to assess the balloon position in the aorta in the port-access.

Postoperative Management:

In uncomplicated minimally invasive cardiac surgery, there is **no need for intensive care unit overnight** residence as **a 4-8 hour post-anesthetic care unit (PACU) stay, followed by** transferring the patient to **a monitored bed** on a surgical nursing unit, is sufficient.

N.B.: **Minimally Invasive (CPB) Cardiac Surgery** includes:
1- MIDCAB and the other incisions.
2- Port-Access.

5- Miniature Axial Flow Pumps

Idea:

Temporary placement of **a miniature pump in the left ventricle** can facilitate coronary grafting, without the need for a CPB circuit. It allows continuous non-pulsatile flow. Still its benefits over OPCAB or MIDCAB are unclear. It may provide hemodynamic support for patients with poor left ventricular function. Impella is an example of these pumps (see before).

6- Arterial Conduits

The coronary artery bypass graft is now chosen as an arterial graft. It is either:
- **The internal mammary artery (IMA) graft:** It has a higher patency rate than vein grafts because it rarely develops atherosclerosis due to:
  - endothelial function and other anatomical differences and
  - high flow in the IMA.
- **The radial, gastro-epiploic or inferior epigastric artery:** They have greater long term patency than vein grafts.

Anesthetic Problems

1- Choice of the Intravenous/Arterial Cannula Site:

Avoid sites of artery or vein grafts. Preoperative communication with the surgeon is important.

2- Prevention of Spasm of arterial conduits is performed by:

- **Diltiazem infusion** of a low dose of 70 μg/min or about 5 mg/h. The infusion is begun as the harvesting (taking-off the graft) begins and is replaced by oral diltiazem in the postoperative period.
- **Nitroglycerin infusion:** A recent report suggests that it is a better choice.

7- Reperfusion Injury

Definition:

It is metabolic, functional, and structural changes after restoration of coronary perfusion, which can lead to additional cellular injury that further augments the ischemic state of injury. Reperfusion injury can be reduced or prohibited by modification of the reperfusion conditions.

Types and Causes:

a) Non-Lethal Reperfusion Injury (Myocardial Stunning):

It is **a transient fully reversible** left ventricular dysfunction (detected by segmental wall motion abnormalities) that persists after reperfusion (**for hours to days**) i.e., delayed recovery with:

- Absence of irreversible damage (mild sub-lethal cellular injury).
- Restoration of normal or near-normal coronary flow (abnormal function with normal or near normal flow) i.e., **flow-function mismatch or uncoupling.**

Myocardial stunning is discussed in full details in the chapter of "Cardiovascular Diseases".

b) Lethal Reperfusion Injury:

It is associated with irreversible cell death (i.e., myocardial necrosis and infarction). The flow is preserved, but the function is reduced (i.e., flow-function mismatch). It is divided into:

1- Early Lethal Reperfusion Injury:

It occurs **immediately** at the beginning of reperfusion during the initial phase of reperfusion.

Causes:

- **Ca^{++} and O_2 paradox:** Reperfusion injury is mainly caused by the consequences of ischemic **calcium overload** together with the re-supply of energy that trigger several critical intra-cellular events including **activation of cellular enzymes and over-activation of the contractile apparatus**.
- Changes of intracellular pH and osmolarity.
- Increased sacrolemmal fragility.

2- Delayed Lethal Reperfusion Injury:

It occurs **later** during the time course of reperfusion.

Causes:

- **Adhesion and activation of neutrophils**; they are activated and **release a variety of mediators** including **O_2 derived free radicals.**
- Adhesion and activation of platelets.
- Activation of the complement system
- Apoptosis.

Effects of Anesthetics on Reperfusion Injury

a- Volatile agents e.g., halothane, enflurane, isoflurane, sevoflurane, desflurane, and xenon (1 MAC for the first 15 min of reperfusion after coronary occlusion) have a cardio-protective effect against reperfusion damage. The mechanism of this protection includes:

- These volatile agents interact with the sarcoplasmic reticulum ryanodine receptors of reperfused heart cells.
- They also reduce secondary reperfusion injury caused by activated leukocytes.

b- Intravenous anesthetic agents: They have little cardio-protective effect during ischemia-reperfusion injury.

8- Myocardial Preconditioning

It was first discovered by Murry and Co-workers in 1986.

Definition: **A brief period of ischemia (like during angina) confers relative protection against a subsequent more prolonged ischemic insult** in human.

Most cells have an endogenous protection system that, if activated before ischemia, partially protects the cells against the consequences of ischemia-reperfusion. The protection mechanism is called "preconditioning".

Activating Stimulus (Triggering Causes of the Preconditioning):

a- Ischemic preconditioning: **A short period of ischemia** that precedes longer periods of ischemia sufficient to induce infarction. Typically, the short periods are consequences of **5-15 minutes of ischemia**

followed by 5 minutes of reperfusion. Most animal models use 4-5 cycles of ischemia and reperfusion after which infarct sizes are reduced by 50% or more. The use of **brief occlusion of a coronary artery** 5-15 minutes, 4-5 cycles, before grafting is done when CABG is being done without CPB i.e., OPCAB. The optimal period of occlusion and the recovery period have not yet been defined.

b- Non-ischemic preconditioning:

- **Oxidative stress.**
- **A small change in temperature.**
- Some anesthetic drugs such as **volatile agents** (the most common is by using 0.1-0.5 MAC for 5-10 minutes) and **xenon, opioids, and propofol**, and non-anesthetic drugs as **adenosine**.

Mechanisms of Preconditioning:

The biochemical basis for this phenomenon is only partly understood. The protective effect of anesthetic preconditioning is mediated by opening of the ATP regulated K^+ channels (K_{ATP} channels) of the mitochondria, which also mediates the protective effect of ischemic preconditioning.

Phases:

Cardiac protection due to preconditioning occurs in 2 phases:

1) Classic or Early Preconditioning (Early Phase of Protection):

Cardio-protection begins shortly after application of the preconditioning stimulus and disappears after 2-3 hours.

2) Late Preconditioning (Second Window of Protection):

Cardio-protection reappears 12-24 hours after the initial preconditioning stimulus, and lasts for 2-3 days (figure 25-26).

Effects of Anesthetics on Late Preconditioning:

The late ischemic preconditioning is augmented by anesthetic preconditioning as follows:

- Five minutes **sevoflurane** inhalation before a prolonged ischemia reduces the infarct size by 50% in already late preconditioning (in animal and human studies).
- Ten minutes **isoflurane** inhalation, at one MAC, before aortic cross-clamping and cardioplegic arrest during CABG surgery reduces myocardial infarcts size (measured by troponin). This is called **pharmacologic preconditioning** with protection similar to that obtained from a brief period of ischemia.

Blockade of Cardio-protection of Preconditioning

a- Barbiturates (at supra-therapeutic doses) and R (-) isomer and racemic ketamine (at clinically relevant doses): They block K_{ATP} channels in cardiac cells and **prevent the cardio-protective effect of ischemic preconditioning.**

N.B.: S (+) ketamine, propofol, etomidate, midazolam, and dexmedetomidine have no effects on K_{ATP} channels.

b- Glibenclamide (an oral sulphonylurea hypoglycemic drug): It blocks K_{ATP} channels in cardiac cells; therefore, Type II diabetes and coronary artery disease may benefit from changing the treatment to insulin.

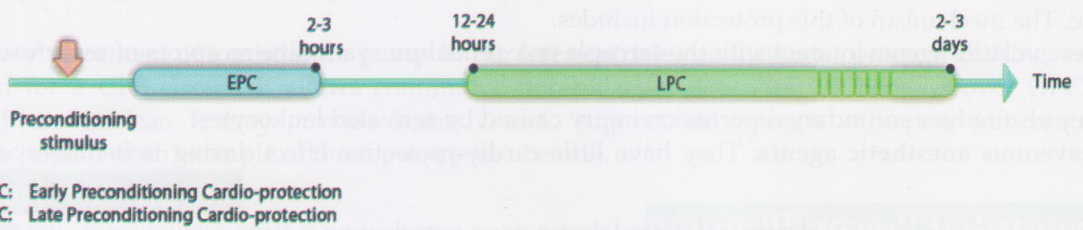


Figure 25-26: Phases of preconditioning

Other Forms of Preconditioning

Postconditioning: It refers to introduction of the protective intervention immediately before or during reperfusion e.g., at the time of release of the aortic cross-clamp during cardiac surgery.

Remote Preconditioning: It refers to a protective effect induced by preconditioning in a remote vascular bed e.g., renal or cerebral protection derived from myocardial preconditioning

N.B.: Preconditioning is described also in the brain as a method of brain protection. It is discussed in chapter "Central Nervous Diseases".

9- Surgical Ventricular Restoration (USA term) or Dor Procedure (European term)

Principle:

• It involves exclusion of the dead portion of the antero-septal and apical areas of the heart leading to a more elliptical geometry (rather than the spherical shape) of the heart. The **elliptical shape is better than the spherical shape** as it **makes left ventricular contraction more efficient improving left ventricular ejection fraction by 10-20%.** In the same time, the antero-septal and anterior apical areas of the heart are **not subjected to form an aneurysm** by this procedure.

N.B.: The spherical shape of the heart is seen in cases of:

- diffuse cardiomyopathy.
- end-stage triple-vessel coronary artery disease causing an extensive antero-septal myocardial infarction.

Surgical Technique:

The operation involves opening the left ventricle vertically, parallel to the inter-ventricular septum, determining the margin of the viable myocardium, encircling the left ventricle cavity from inside with a purse-string suture, sewing in an ovoid ring that typically contains Dacron or bovine pericardium, then closing the non-viable ventricle over the newly constructed synthetic left ventricular apex.

Anesthetic Management:

1- The **patient** is usually with **left ventricular ejection fraction of <30%** and has symptomatic **congestive heart failure**.

2- Preoperative medications as **angiotensin converting enzyme inhibitors (ACEIs), β-blockers, diuretics, or digoxin** should be taken.

3- **Implanted Cardioverter-Defibrillators and pacemakers** (if present) should be deactivated pre-operatively and reactivated postoperatively.

4- Monitors:

- Continuous cardiac output and/or mixed venous O_2 measurement by **a pulmonary artery catheter.**
- **Trans-esophageal echocardiography** is essential to:
  - help the surgeons locate the apical patch optimally by analyzing left ventricular wall motion.
  - detect the need for mitral valve repair or replacement.
  - assess the inferior left ventricular wall motion after CPB.
  - assess presence of leak around the patch.
  - assess left ventricular preload because left ventricular function is impaired.

5- **CPB** is needed during this procedure.

6- After CPB; **optimization of the rhythm, preload, afterload, and contractility** is needed.

- Assuming there is no active myocardial ischemia, a heart rate between 90-100 is optimal with the stroke volume of the freshly shrunken left ventricular cavity as it begins gradual remodeling.
- Inotropic support (as dobutamine, epinephrine, or milrinone) is needed.
- Vasopressors are used. If there is decreased systemic vascular resistance, vasopressin is preferred to norepinephrine as it preserves the renal blood flow.
- Nesiratide (a natriuretic peptide): It maintains cardiac output and urine output, but decreases mean arterial blood pressure.
- An intra-aortic balloon pump is needed in 8% of cases.

10- Trans-myocardial Laser Revascularization and Stem Cell Therapy

Indications:

1- Patients who have diffuse coronary artery disease and who cannot be completely revascularized by CABG alone. In 10-25% of CABG, incomplete revascularization occurs, which can cause recurrent chest pain early, and late death.

2- Patients who have disabling, medically refractory, severe angina.

Technique and Action:

• TMR is done via a thoracotomy or using a minimally invasive technique. TMR, through the laser channel, creates a localized area of injured heart muscle cells, which during their repair stimulates new blood vessel growth or angiogenesis.

• It has been demonstrated that injection of biologics such as **stem cells or growth factors** at the time of creating the laser channel enhances angiogenesis beyond the effect that either TMR or stem cells will have

by themselves. The inflammation caused by the TMR channel provides a "fertile" area for enhanced stem cell uptake and angiogenesis.

N.B.: Stem Cell Therapy

It is the use of stem cells in surgical procedures as in cardiac, peripheral vascular, neurological, orthopedic, and hepatic surgeries.

Disadvantages:

1- Ethical problems: because stem cells are obtained from embryos after killing them.
2- The inability to efficiently culture or isolate them outside the laboratory.

Technique (approved by Food and Drug Administration):

- An autologous bone marrow stem cell isolator (HARVEST) is used now to isolate stem cells. In this technique, the bone marrow is collected in the operating room at the time of surgery and by using the HARVEST system, bone marrow is separated into its different parts in a process that takes only 15-20 minutes.
- The patients own sterilely concentrated stem cells that can then be utilized in an efficient and timely manner during surgery in a safely utilized way.

Extra-Corporeal Membrane Oxygenation (ECMO)

It is a **prolonged** extracorporeal **CPB** achieved by **extra-thoracic vascular cannulation**. It is a modified heart lung machine **consisting of:**

- a distensible venous blood drainage reservoir,
- a roller pump,
- a membrane oxygenator: to exchange O_2 and CO_2, and
- a heat exchanger: to maintain temperature.

The patient must be maintained on **continuous heparin anticoagulation** to prevent thrombosis within the circuit.

Indications

A) Cardiac Indications of CPB:

1- CABG.
2- Port-Access CABG and MIDCAP.
3- Chronic constricting pericarditis.
4- Valve replacement.
5- Congenital heart diseases.
6- Cardiac transplantation.
7- Post-cardiac arrest.
8- Surgical ventricular restoration surgery (Dor procedure).

B) Non-Cardiac Indications of CPB:

1- Persistent Fetal Circulation (Persistent Pulmonary Hypertension of the Newborn):
The primary cause might be
- **Primary** persistent fetal circulation.
- **Congenital diaphragmatic hernia.**
- **Meconium aspiration.**
- **Acute respiratory distress syndrome.**
- **Sepsis.**

Regardless the primary cause, CPB is used in patients who have potentially reversible underlying pathological process (e.g., acute reversible respiratory or cardiac failure) not responding to the optimal ventilatory and maximal pharmacological management.

2- Acute Respiratory Failure and Acute Respiratory Distress Syndrome (ARDS):
It is used in patients who have potentially reversible underlying pathological process not responding to the optimal ventilatory and maximal pharmacological management.
Value of ECMO in respiratory failure:

- **It reduces lung injury** associated with mechanical ventilation.
- O_2 and CO_2 gas exchange takes place during ECMO at ventilator settings that **rest the lung** (in newborns and adults).
- **Systemic perfusion is well supported.**

Its results in ARDS are not promising.

3- Liver Transplantation.

4- Renal Surgery: Renal cell carcinoma extending into the inferior vena cava or right atrium.
5- Pulmonary (Thoracic) Surgery:
- **Left sleeve pneumonectomy** with clamshell incision.
- **Lung transplantation** (single or double).
- **Broncho-pulmonary lavage** in children for **pulmonary alveolar proteinosis**.

6- Neurosurgery for a huge aneurysm.
7- Tracheal Surgery:
- A **laryngo-tracheo-esophageal cleft.**
- **Tracheal resection** (especially **carinal resection**).

8- Vascular Surgery:
- **Advanced arterio-venous malformation**.
- Surgery on the **descending thoracic and thoraco-abdominal aorta**.

9- Shock:
- **Septic** shock.
- **Cardiogenic** shock.

10- Malignant Hyperthermia as a method of cooling.

Contraindications of ECMO

a- Neonates:

1- Premature neonates (birth weight < 2 kg or gestational age < 35 weeks) because intracranial bleeding occurs primarily in premature neonates.
2- Evidence of **intracranial hemorrhage** or other brain damage.
3- Multiple congenital anomalies.
4- Congenital heart disease.
5- Irreversible lung damage.

Therefore, neonates who are potential ECMO candidates should be evaluated by:
- Cranial ultrasound to rule out intracranial hemorrhage.
- Cardiac ultrasound to rule out congenital cardiac anomalies.

b- Adults:

1- Potential **bleeding complications**.
2- **Irreversible lung damage.**

Types of ECMO

A- Venoarterial ECMO:

It is the one most commonly used. The venous catheter is threaded via the **right internal jugular vein** down to the **right atrium or the femoral vein.** It is used for drainage as it carries blood to the oxygenator. The arterial catheter is threaded via **the right common carotid artery** down to **the aortic arch** or **femoral artery**. It is used for re-infusion.

Advantages:

1- It **allows lung rest** from the harmful effects of excessive positive pressure ventilation (pulmonary barotraumas, O_2 toxicity) by reduction of ventilatory settings (peak inspiratory pressure, FiO_2, respiratory rate, and positive end-expiratory pressure "PEEP").

2- **It diverts** as much as **80% of the cardiac output** from the right atrium to the extracorporeal circuit **reducing** or eliminating the **right to left shunt** through a patent foramen ovale or patent ductus arteriosus, which **closes** spontaneously during the course of ECMO. If it does not close, surgical closure is indicated while the patient is on ECMO.

3- **It decreases pulmonary blood flow and pulmonary artery pressure,** which decreases **right ventricular work**.

4- **It corrects arterial hypoxemia and acidosis,** which decreases pulmonary vasoconstriction (also, it improves the systemic oxygenation and decreases the ductal flow, which enhances spontaneous ductal closure).

5- It allows **rapid growth of the hypoplastic lung** in patients with congenital diaphragmatic hernias.

B- Venovenous ECMO (Extracorporeal membrane CO_2 Removal):

The first venous catheter is threaded via the **right internal jugular vein** down to the **right atrium.** It is used for drainage as it carries the blood to the oxygenator. The second venous catheter is threaded via **the right femoral vein**. It is used for re-infusion. Sometimes, a double-lumen polyurethane catheter is used for **single-site cannulation of the right internal jugular vein.**

Advantages:

1- **It allows lung rest** by reducing the motion of the diseased lungs and preventing their damage. This is accomplished by **low frequency positive pressure ventilation** (in addition to 3-5 sighs/min to preserve functional residual capacity).

Oxygenation is accomplished **by the lungs** while the extracorporeal circuit is used for CO_2 removal. This combination of low frequency ventilation and **CO_2 removal by ECMO** is performed at an extracorporeal blood flow rate of 20%-30% the cardiac output.

Total gas exchange can be achieved by the venovenous circuit (if the lung is non-functioning) by increasing the extracorporeal blood flow rate to 120% the cardiac output.

2- **Maintenance of pulmonary blood flow**.

3- **Avoids the risks of arterial cannulation.**

C- Veno-Venous Arterial ECMO:

The first venous catheter is threaded via the right internal jugular vein or the femoral vein. It carries the blood to the oxygenator. The second catheter is threaded to the internal jugular vein and the femoral artery.

Complications of ECMO

After 20 days of ECMO support, the complications may exceed the potential benefits.

1- Mechanical Complications: more common in adults.

- Circuits: ▫ **Clots** in the circuits.
  ▫ Air in the circuits and **air embolism.**
  ▫ **Cracks** in the connectors.
  ▫ **Rupture**.
- **Malfunction** of the oxygenator, heat exchanger, hemo-filter, or pump.
- **Vascular cannulas**: ▫ **Malposition** requires repositioning.
  ▫ Unintentional **de-cannulation or kink**.

2- Patient Complications: more common in children.

- **Bleeding:** (common)
  ▫ **Intracranial bleeding** especially in **premature neonates** < 2 kg birth weight or < 35 weeks gestational age or patients with **recent head trauma**.
  ▫ **Gastrointestinal and nasopharyngeal bleeding** are more common in adults.
- **Cardiovascular:**
  ▫ Persistent patent ductus arteriosus.
  ▫ Hypoxic cardiac arrest during cannulation (requiring cardiopulmonary resuscitation).
  ▫ Systemic hypertension (requiring vaso-active drugs).
  ▫ Hemo-pericardium and cardiac tamponade.
  ▫ Global myocardial dysfunction.
- **Renal: Acute renal failure** (requiring dialysis or continuous hemo-filtration through the ECMO circuit).

Cardiac Transplantation

Indications

End-stage cardiac disease with ejection fraction usually 20% and severely limited prognosis (i.e., are unlikely to survive the next 6-12 months).

1- Dilated Cardiomyopathy:

It represents > 90% of heart transplants. It is usually due to:

- **Ischemic** cardiomyopathy (44.3%).
- **Idiopathic** cardiomyopathy (43.7%).

2- Other conditions:

They represent < 10% of heart transplants. They include:

- **Graft rejection** i.e., re-transplant (2%).
- End-stage **valve** disease (3.6%).
- End-stage **congenital** heart disease (1.5%).
- Miscellaneous (4.9%).

Criteria for Recipient Selection

1- The patient has one of the above indications. The majority of patients are NYHA class IV status. NYHA class III patients are considered for transplantation when there is a possibility of an abrupt change to class IV status.

2- The recipient should not have any contraindications:

Contraindications are diminished over recent years. They include:

Absolute:

- Neoplasm, with the exception of skin tumors.
- Acquired immunodeficiency syndrome (AIDS).
- Multi-system lupus erythematosus or sarcoidosis.
- **Fixed irreversible pulmonary hypertension**, as it may cause acute right ventricular failure and death after cardiac transplantation; therefore, careful assessment of the pulmonary vascular resistance and trans-pulmonary pressure gradient before and after O_2 and i.v. pulmonary vasodilators is essential. Fixed pulmonary hypertension is associated with:
  - Pulmonary vascular resistance greater than 400 dyne/second/cm^5 (5 wood units).
  - Trans-pulmonary pressure gradient > 15 mm Hg.

  Patients with long standing pulmonary hypertension may be candidates for combined heart-lung transplantation.
- Any systemic illness that would limit survival despite transplant such as irreversible hepatic or renal dysfunction.

N.B.: Reversible hepatic and renal dysfunction are common due to hypoperfusion and venous congestion.

Relative:

- Age over 65.
- Peripheral vascular disease, carotid stenosis (depending on severity).
- Human immunodeficiency virus (HIV), hepatitis B.
- Severe pulmonary disease such as severe chronic obstructive pulmonary disease (COPD), active recent pulmonary infection (< 8 weeks) due to possibility of precipitation of infection from the immuno-suppression.
- Diabetes with end-organ damage; neuropathy, nephropathy, retinopathy.
- Psychosocial impairments; drug or alcohol addiction, smoking, mental defect, history of noncompliance as the patient may not obey the postoperative orders.

Indications of Combined Heart/Lung Transplantation

1- Congenital heart disease (the most common).
2- Primary pulmonary hypertension.
3- Cystic fibrosis.
4- Idiopathic pulmonary fibrosis.
5- α_1 antitrypsin deficiency.

The presence of corpulmonale is not an indication for heart lung transplantation because recovery of right ventricular function is typically rapid and is completed after lung transplantation alone.

Heart-lung transplantation is done by a transverse thoracotomy incision where the donor's heart and lungs are transplanted en bloc.

Alternatives to Cardiac Transplantation (due to a shortage in donors)

1- The use of angiotensin converting enzyme inhibitors (ACEIs) and Carvedilol.

2- Ventricular assist device implantation or semi-implantable peri-corporeal devices, which can be used as follows:
- To allow myocardial recovery (a bridge-to-recovery) especially in young patients.
- To allow a definitive ventricular assist device implantation at a later stage (a bridge-to-bridge).
- To allow time until heart transplantation (a bridge-to-transplant).

Results

Survival rates are:
- 80-90% at one year postoperatively.
- 75% at 3 years postoperatively.
- 60-70% at 5 years postoperatively.
- 50% at 10 years postoperatively.

More than 90% of patients have the chance to return to NYHA class I functional capacity with appreciable improvement in the quality of life.

Criteria for Donor Selection

The donors are **brain-dead persons** most commonly after head-trauma. The donors should have the following criteria:

1- Cardiac criteria: The donor should not have had:

- Prolonged sustained cardiac arrest.
- Prolonged inotropic support.
- Severe chest trauma.
- Intra-cardiac injections.
- Septicemia.
- Coronary artery atherosclerosis.
- Contractile dysfunction.

2- Blood ABO compatibility because its mismatch may result in hyperacute rejection.

3- Body weight should be **within 20%** of the recipient's weight.

4- Hepatitis B, C, HIV, and cytomegalovirus free.

The Donor's Heart Ischemia Time:

It is the time from cross-clamping the aorta at harvesting, to cross-clamp removal after transplant. If it is < **4-6 hours,** it is considered an acceptable limit.

N.B.: Recent researches are directed to: ▫ The possibility of xeno-transplantation especially using porcine.
▫ The preservation of cardiac allograft vasculopathy.

Anesthetic Management for Cardiac Transplantation

Preoperative Management

1- Preoperative Assessment of Cardiac Lesions:

- The patients usually have **heart failure with 20% ejection fraction;** therefore, **complete assessment** is done (history, examination, and investigations) (as before).
- Proper preoperative **management** is important. It is discussed in chapter "Cardiovascular Diseases".
- Patients are usually on diuretics, vasodilators, i.v./oral inotropes, or oral anticoagulants as warfarin .....etc.
- **Mechanical circulatory support** (e.g., intra-aortic balloon pump counter-pulsation, left and/or right ventricular assist devices, or total artificial heart) may be used to sustain life in the moribund patient awaiting a donor heart.

2- Preoperative Assessment of Other Systems:

- Preoperative assessment and management of other systems are important for detection of contra-indications.
- Many patients undergoing heart transplant have abnormal coagulation reflecting passive congestion of the liver due to chronic congestive heart failure.

3- Premedication and Drug Therapy:

Patients presenting for heart transplantation range from those who are compensated and awaiting at home for a suitable heart (on medical therapy as before) to these who are decompensated (and with inotropic support, ventilatory and/or mechanical circulatory support).

1. Sedatives:

- For compensated patients, **small** dose oral benzodiazepines are given.
- For decompensated patients, **no** sedation is given because it blunts the patient's respiratory and sympathetic drive causing hypoxemia, hypercapnia, and even hypotension.

2. Aspiration Prophylaxis:

The compatible donor heart usually becomes available suddenly; so, the patients are considered to have a **full stomach**. There is increased risk of aspiration because of:

- Recent food ingestion before notification of the surgery.
- Delayed gastric emptying.
- Oral administration of cyclosporine A (given preoperatively).

Therefore, antacids (Na citrate), H_2 blockers, and metoclopramide are given.

3. Infection Prophylaxis:

Usually preoperative cephazolin 1 gm i.v. is given (+ postoperative trimethoprim and sulfamethoxazole, acyclovir, and gamma immunoglobulins).

4. Immuno-suppressive Protocol: is usually initiated preoperatively.

- Preoperative methyl prednisolone 0.25 mg/kg/6 h.
- Preoperative oral cyclosporine A.
- Preoperative i.v. azathioprine just before the induction.

4- Patient Preparations:

The same as that in cardiac surgery (see above).

5- Patient Monitoring:

The same as that in cardiac surgery (see above), in addition to the following considerations:

- **Strict aseptic** techniques are used.
- As regards **central venous cannulation**, usually the **left** internal jugular vein is used to preserve the right internal jugular vein for repeated access for heart biopsies after transplantation during the postoperative period.
- As regards **pulmonary artery catheter**, its use is **controversial**. It has advantages and disadvantages:

Disadvantages:

- Theoretical increased **risk of infection, tricuspid regurgitation, coiling, or ventricular irritability.**
- **Lack of any requirement** for pulmonary artery catheter measurement in the absence of pulmonary hypertension.

Advantages: Some physicians find pulmonary artery catheter very useful during discontinuation of CPB and in the postoperative period due to:

- **Pulmonary vascular resistance** is almost always high in patients with cardiomyopathy and it is important to **decrease it to avoid right-sided heart failure** in the transplanted heart. This is obtained only by a pulmonary artery catheter.
- Recently, a **modified right ventricular ejection fraction catheter** is inserted, that monitors the right ventricle and can demonstrate the need for postoperative pharmacological support of the right ventricle.
- An **oximetric pulmonary artery catheter has many advantages.**

N.B.: It is necessary to withdraw the central venous or pulmonary catheter into the superior vena cava when the heart is removed. The catheter is then repositioned into the donor heart.

- **Trans-esophageal echocardiography** is usually used to monitor cardiac function.

Intraoperative Management

Proper timing and coordination are needed between the donor organ retrieval team and the transplant center because:

- Premature induction unnecessarily prolongs CPB.
- Delaying induction jeopardizes the graft function, by prolonging the donor's heart ischemia time, which is limited to 4-6 hours.

Complete aseptic techniques are used e.g., airway equipment such as:

- **Sterile anesthetic delivery tubing and handling with sterile gloves.**
- **Bacterial filters** are often used on the inhaled and exhaled limbs of the anesthetic delivery tubing.

Anesthetic aim

To control the hemodynamic stability in patients who have little or no cardiac reserve.

Induction

Modified rapid-sequence induction is applied:

- Preoxygenation with 100% O_2 for 5 minutes.
- Vecuronium 0.5 mg/kg i.v. or **rocuronium** 0.6 mg/kg i.v. (**succinylcholine** can be used). Avoid muscle relaxants, which cause histamine release.
- **Fentanyl** 10-15 µg/kg i.v. or **sufentanil** 2-7 µg/kg i.v. ± **midazolam** 15-70 µg/kg i.v.
- Cricoid pressure and slight head-up position should be maintained during intubation to decrease aspiration.

Etomidate is of choice as it has little effect on hemodynamics. Other agents such as thiopentone, ketamine, and midazolam can be used.

Hypotension is common after induction, and is managed with inotropes, vasopressors, and fluids.

A **trans-esophageal echocardiography probe** is placed after induction.

Maintenance

The same as open cardiac surgery (see above), in addition to the following considerations:

- N_2O may be used with O_2 (6: 4) to keep the patient unconscious, but must be omitted before CPB to avoid potential air microemboli. N_2O is usually not used especially in:

- Patients with increased pulmonary vascular resistance because it causes pulmonary vasoconstriction (N_2O abolishes the hypoxic pulmonary vasoconstrictive reflex).
- Patients with severe cardiac decompensation because it causes additive depressant effects with opioids.

• Muscle relaxants with **little cardiovascular effects** such as vecuronium are preferred. Some prefer pancuronium as it counteracts opioid induced bradycardia.

• Mechanical ventilation should be stopped during sternotomy to deflate the lungs to avoid lung injury from the electric saw.

Prebypass and Bypass Periods

The same as open cardiac surgery (see above), in addition to the following considerations:

1- **Diuretic therapy** may be needed during CPB to maintain urine output because most transplant patients require diuretic therapy before the surgery.

2- If the **central venous catheter or pulmonary artery catheter** has been used, it should be **withdrawn** out of the heart at 20 cm position into an 80 cm protective sterile sleeve and should be withheld in the vena cava, before the snares around the caval cannulas are tightened. They can be **re-inserted through the donated heart** (with the aid of the surgeon from the operative field) before discontinuation of the CPB.

3- **During the procedure:**

• The recipient's heart is then excised leaving **the posterior wall of both atria (with the caval and pulmonary vein openings).**

• The atria of the donor's heart are **anastomosed** to the recipient's atrial remnants **(left side first)**, and the sino-atrial node is preserved.

• Then the **aorta** is anastomosed first, followed by end-to-end **pulmonary artery anastomosis** to allow earlier removal of the aortic cross-clamp.

• The heart is then **flushed with saline** and intra-cardiac air is evacuated.

• **Methyl prednisolone** is given before the aortic cross-clamp is released.

Termination of CPB

The same as open cardiac surgery (see above), in addition to the following considerations:

1- Re-warming Period:

A **longer** re-warming period is required due to:

• more profound cooling of the donor's heart and

• more prolonged ischemia time than usual cardiac operations.

2- Chronotropic Support:

Because the transplanted heart is denervated, it typically develops **sinus bradycardia or atrio-ventricular block** during weaning from CPB and requires:

• **Isoprenaline (isoproterenol) infusion:** 0.01-0.05 µg/kg/min is routinely initiated before discontinuation of CPB to:
- maintain the heart rate at 100-120 beat/min.
- augment the performance of the transplanted heart, as it maintains cardiac output.

• **Epicardial pacing** that may be needed.

3- Inotropic Support:

Such as adrenaline, nor-adrenaline, or amrinone that may be used to augment a poorly contracting right ventricle.

4- Reduction of Pulmonary Vascular Resistance

See later.

Post-bypass Period

The same as open cardiac surgery (see above).

Postoperative Management and Intensive Care Considerations

The same as open cardiac surgery (see above) except application of fast-tracking management.

Postoperative Complications:

The same as open cardiac surgery (see above), in addition to the following complications:

A) Cardiovascular Complications:

1- Pulmonary Hypertension (Right Ventricular Failure)

It is one of the major causes of **early mortality** (0-2 days).

Mechanism: abrupt and persistent increase in pulmonary vascular resistance resulting in an increased afterload on the newly implanted heart. This is augmented by:

- The heart being **post-ischemic** i.e., with decreased cardiac index, decreased diastolic function, and increased filling pressure resulting in a relatively fixed stroke volume and cardiac output, which is heart rate dependent.
- The heart being denervated; therefore,
  - Sino-atrial (SA) node and atrio-ventricular (AV) node dysfunction cause severe bradycardia and heart block.
  - The transplanted heart is isolated from the baroreceptor reflex. It is unable to increase the heart rate and cardiac output in response to hypovolemia i.e., pre-load dependent.

Management

1. Decrease the pulmonary vascular resistance by:

- **Hyperventilation.**
- **Prostaglandin E_1** (PGE_1) infusion: 0.025-0.2 µg/kg/min.
- **Prostacyclin (PGI_2)** infusion: 0.16 µg/kg/min.
- **Nitric oxide** inhalation: 10-40 ppm.
- **Isoprenaline infusion.**
- **Phosphodiesterase inhibitors** as amrinone or milrinone: They produce systemic and pulmonary vasodilation, and inotropic action.
- **Nitrates.**

2. Improve the right ventricular function by:

- **Inotropes** e.g., nor-adrenaline, amrinone...etc.
- **Right ventricular assist devices.**

N.B.: Causes of early graft (heart) failure: (22% of causes of deaths).

- Unknown especially while the patient is still in the operating room.
- Pulmonary hypertension.
- Right ventricular failure.
- Hyper-acute rejection.

2- Arrhythmias: are either:

- **Brady-arrhythmias and heart** block, which may require **a permanent pacemaker**.

N.B.: AV node dysfunction may resolve spontaneously within 48 hours, but SA node dysfunction may persist in 5% of transplant patients.

- **Lack of vagal tone of the denervated heart** increases the heart rate up to 100-120/min.

3- Post-Transplanted Bleeding:

The same causes as open cardiac surgery (see above), in addition to:

- Extensive suture lines that increase the risk of anastomosis leaks.
- Bronchial artery injury especially with pulmonary hypertension, which causes dilatation of the bronchial artery.

It is responsible for 6% of causes of death.

4- Allograft Coronary Artery Disease (Cardiac Allograft Vasculopathy)(CAV):

Coronary artery disease (accelerated atherosclerosis) occurs in 10% of patients during the first year, and in 50% during the 5 postoperative years due to the following:

- Some **coronary arteries, which are diseased** are transplanted with the donor's heart.
- **Immunological injury** to the vascular endothelium.
- **Ischemic injury** at the time of transplantation.
- Other **risk factors** e.g., hypertension, smoking, diabetes mellitus, female donor, female recipient, and congenital heart disease.

Allograft coronary artery disease is usually silent due to lack of afferent innervations; so, ECG diagnosis and follow up angiography are mandatory.

B) Postoperative Rejection

Types of rejection

1- Hyper-acute Rejection:

It occurs within **hours**. It occurs because of **preformed human Leukocytic antibodies** (HLA) in the recipient's serum that are specific for the donor HLA, due to prior exposure to HLA via:

- Prior blood transfusion.
- Pregnancy.

- Prior transplantation.

It is very rare and has a poor response to any combination of therapies.

2- Acute Rejection:

It occurs within **days or weeks** (maximum rejection rate occurs in the first 3 months). It is mediated through **T-lymphocytes response** to the donor's heart.

Clinical Picture:

- Asymptomatic.
- Symptoms of right ventricular failure (may be due to other factors, but should be considered to be due to acute rejection until proven otherwise).

Investigations:

- ECG shows low voltage QRS complexes.
- Repeated transvenous endomyocardial biopsies (the most important) show right ventricular cellular infiltrate. It provides early warning. Sampling errors may occur due to:
  - Non-homogenous cellular infiltrate of the right ventricle.
  - Presence of scar tissue from repeated biopsies.
- Repeated Doppler echocardiography shows shortening of the isovolemic relaxation period or an onset of a restrictive pattern of left ventricular filling.
- Magnetic resonance imaging (MRI).
- Cyto-immunological study.

3- Chronic Rejection:

It occurs in 40-50% of patients, **5 years** after transplantation.

Pathology:

- Fibro-intimal proliferation.
- Diffuse vessel involvement.
- Small intra-myocardial arteries.
- Concentric intimal thickening.
- Absence of calcification.

Clinical Picture:

- Coronary arteriosclerosis.
- Arrhythmias. Sinus bradycardia and atrio-ventricular block are early signs of rejection, although rejection may be associated with any arrhythmias.
- Silent myocardial infarction (painless infarction as the heart is denervated). However, limited sympathetic nervous system function and re-innervation of the transplanted heart occur usually within 6-12 months; so, painful myocardial ischemia (angina) is possible.
- Decreased exercise tolerance.
- Congestive heart failure.
- Sudden death may occur.

Treatment:

- Periodic evaluations including percutaneous trans-luminal coronary angioplasty.
- Re-transplantation.

Immuno-suppressive Therapy:

- It consists of cyclosporine A, azathioprine, anti-thymocyte globulin, and prednisone.
- Rejection episodes are treated with oral or i.v. corticosteroids.
- Refractory rejection has been treated with OKT-3 successfully.

N.B.: Heart-lung recipients usually present with pulmonary rather than cardiac rejection.

C) Postoperative Infection:

Nearly 50% of all first year deaths are infection related **(the most common cause of death).**

Due to: **chronic immuno-suppression** increasing the susceptibility to opportunistic infection.

Types:

- Bacterial: especially in lungs.
- Viral: cytomegalovirus, herpes simplex, and herpes zoster.
- Fungal: candidiasis.
- Protozoal: pneumocystis carinii.

Prevention:

- **Avoid nasal intubation** because it is associated with infection by diphtheroids and staphylococcal commensals from the nasopharynx and skin.

- Trimethoprim, acyclovir, pneumococcal vaccine, sulfamethoxazole, and gamma immunoglobulins can be used.

N.B.: The most common causes of deaths include:

- Infections.
- Acute heart failure.
- Severe pulmonary hypertension with secondary right ventricular failure.
- Early allograft rejection.
- Post-transplant bleeding.

Anesthesia for a Patient with a Transplanted Heart

The number of patients with cardiac transplants has increased due to:

- Increased frequency of transplantation.
- Increased survival rates.

This makes it increasingly likely that they present for non-cardiac surgery outside a specialist center.

These patients may present to the operating room either:

a- Early in the postoperative period for: ▫ Mediastinal exploration.
▫ Re-transplantation.

b- Late after the postoperative period for ▫ Incision and drainage of infections.
▫ Unrelated surgeries.

Pathophysiology of the Transplanted Denervated Heart

The recipient's atrium remains innervated, but hemodynamically unimportant, whereas the donor atrium is denervated (i.e., it is **devoid of all normal autonomic innervation**) and is responsible for the electro-physiological responses of the transplanted heart.

a- Absence of Sympathetic Innervation:

- The transplanted heart is **depleted of adrenaline and nor-adrenaline** due to interruption of post-ganglionic cardiac nerves.
- The transplanted heart **retains its normal intrinsic control mechanism** such as:
  - ▫ Normal Frank-Starling effect.
  - ▫ Normal impulse formation and conductivity.
  - ▫ Intact α and β receptor responses; actually there is **β -adrenergic receptor up regulation.** This results in postsynaptic β adrenergic receptor **hypersensitivity** causing **normal or even increased response to circulatory catecholamines.**

b- Absence of Parasympathetic Innervation:

The transplanted heart is **isolated from the baroreceptor control loop**.

Due to absence of sympathetic and parasympathetic innervation of the heart, the following effects can occur:

1- The Heart Rate:

- **Resting heart rate** is **90-110 /min** (similar to the heart rate with both vagal and β receptor blockade) due to the intrinsic rate of the donor's SA node discharge.
- During exercise: ▫ **Chronic exercise** causes **a slight decrease in the resting heart rate**.
  - ▫ **Acute exercise** causes **a delayed increase in the heart rate, and a delayed decrease in the heart rate** after completion of exercise due to time needed for release and destruction of circulating catecholamines.
- **Drugs** which affect the heart rate (i.e., affect the vagal tone) have **no effect on the transplanted heart rate e.g., atropine, opioid, neostigmine, edrophonium, suxamethonium, pancuronium, and digoxin.**
- There is **no sympathetic response to direct laryngoscopy and tracheal intubation** and the denervated heart has a blunted heart rate response **to light anesthesia or intense pain**.
- During hypovolemia or hypotension, the **denervated heart lacks the ability to respond acutely with reflex tachycardia**, but responds to stress primarily by an increase in stroke volume (due to intact Frank-Starling mechanism). This is due to the effect of endogenous catecholamines on the SA node with absence of control via neural mechanisms. Therefore, **the transplanted heart is preload dependent and venous return dependent** until heart rate increases after several minutes in response to the circulating catecholamines (due to intact α and β receptors).

• The normal respiratory variations, response to carotid sinus massage and to Valsalva maneuver are absent.

• About **25%** of patients develop **bradycardia** after-transplantation that requires β-agonist or insertion of a permanent cardiac pacemaker. First-degree AV block is common. Supraventricular tachyarrhythmias (treated by verapamil, procainamide, and quinidine) and ventricular arrhythmias (treated cautiously by lidocaine due to its negative inotropic action) can occur.

2- Cardiac Output:

The cardiac output during the immediate postoperative period is decreased or low normal and there is a **delayed increase in the heart rate** in response to exercise, because the response is dependent on the increase in circulatory catecholamines i.e., there are:

- Decreased cardiac index.
- Decreased diastolic compliance.
- Increased right ventricular and left ventricular filling pressure (which gradually decrease).

Because the starling relationship between end-diastolic volume and cardiac output is normal, cardiac output is preload dependent.

3- Coronary Autoregulation is preserved.

4- Disturbed pulmonary lymphatics make these patients very susceptible to **pulmonary edema**. Strict attention to maintaining euvolemia is therefore vital.

Anesthetic Management

Preoperative Management

1- Preoperative Evaluation of the Cardiovascular System for cardiovascular complications as before e.g., pulmonary hypertension, rejection, allograft coronary artery disease…etc.

2- Preoperative Evaluation of Other Systems especially the blood volume (because the heart is preload dependent) postoperative infections…etc.

3- Medical Therapy for:

Complications of immuno-suppression e.g., cyclosporine, corticosteroids…etc. such as renal impairment and hypertension. The immunosuppressive therapy is discussed in chapter "Pharmacological Adjuncts for Anesthesia & Intensive Care".

Intraoperative Management:

Choice of Anesthesia

Nearly **all** anesthetic **techniques** including regional anesthesia have been used successfully in transplanted patients.

Anesthetic Problems:

1- Spinal or Epidural Blocks:

Some physicians avoid spinal or epidural blocks due to their association with hypotension, which is undesirable.

2- Cardiac Output:

Maintain a normal or high cardiac **preload** because the heart is preload dependent. So, intraoperative fluid infusion should be maintained carefully. Vasopressin may be needed to treat severe hypotension unresponsiveness to catecholamines.

3- Heart Rate:

• The patient is **very sensitive to rapid vaso-dilatation** e.g., spinal anesthesia, due to absence of reflexes, which increase the heart rate; therefore,

- **Isoproterenol, glucagon, dopamine, dobutamine, or diluted epinephrine** should be readily available to increase the heart rate if necessary as they act as expected.
- Indirect **vasopressors** e.g., ephedrine have blunted effect and are less effective than **direct-acting agents** due to absence of catecholamine stores in myocardial neurons.
- Hydralazine and phenylephrine produce no reflex tachy- or bradycardia in response to their primary actions.

• The heart rate is **not affected by**:

- Opioids and cholinesterase inhibitors (which originally decrease the heart rate).
- **Anticholinergics and pancuronium** (which originally increase the heart rate), but still **anticholinergics** must be **given to:**
  - **Reverse muscle relaxants** to block the non-cardiac muscarinic effects of acetylcholine.

- **Block the cardiac side effects (decreased heart rate)** due to the possibility of **slow development of cardiac re-innervation** especially in remotely transplanted patients (> 6 months).
- Digoxin or nifedipine.

• Arrhythmias may occur as above.

4- Monitoring:

Besides the standard monitors, the following considerations should be taken:

• The **ECG** monitor is carefully examined for **ischemia. Two sets of P waves** are present. One representing the recipient's own SA node (which is left intact) and the other representing the donor's SA node. The recipient's native SA node may still be affected by autonomic influences, but it does not affect the cardiac function, its effect cannot traverse the suture line, and it has no effect on the chronotropic activity of the heart.

• Invasive monitors such as **invasive blood pressure, central venous catheterization, and pulmonary artery catheterization** for major procedures should be performed with **strict asepsis** during placement. Trans-esophageal echocardiography is an alternative to invasive monitors.

Pericardial Diseases

• Normally, the pericardium is formed of:
- Parietal pericardium, which is a stiff fibrous membrane surrounding the heart.
- Visceral pericardium, which is closely related to the heart.

• The pericardial sac lies between the two layers; it contains 20-50 mL of pericardial fluid normally in adults (an ultra-filtrate of plasma).

• Intra-pericardial pressure (as pleural pressure) is sub-atmospheric, which decreases on inspiration (- 4 mm Hg) and increases on expiration (+ 4 mm Hg).

• The function of the pericardium is:
- to limit acute dilatation of the ventricles.
- to allow diastolic coupling of the two ventricles i.e., distention of one ventricle interferes with the filling of the other.

• Pericardial diseases include:
- Acute pericarditis.
- Chronic constrictive pericarditis.
- Pericardial effusion.
- Cardiac tamponade.

Acute Pericarditis

It is an inflammatory process of the pericardium with/without pericardial effusion.

Causes:

1- Infectious: viral (the most common), bacterial, fungal, tuberculosis (usually with human immunodeficiency virus).

2- Post-myocardial infarction (Dressler's syndrome). It occurs after acute myocardial infarction by several weeks. It is thought that Dressler's syndrome is the result of an autoimmune process that is initiated by the entry of necrotic myocardium into the circulation where it acts as an antigen.

3- Post-traumatic e.g., after cardiac surgery (acute pericarditis occurs then pericardial effusion occurs and reaches its maximum at the 10th day then gradual regression occurs), pacemaker application, intra-cardiac catheters, or diagnostic procedures.

4- Metastatic diseases.

5- Drug-induced (minoxidil or procainamide).

6- Mediastinal radiation.

7- Systemic diseases as rheumatoid arthritis, systemic lupus erythematosus, scleroderma, **uremia**...etc.

8- Idiopathic (the most common).

Clinical Picture:

If acute pericarditis is transient and is not complicated by pericardial effusion, cardiac tamponade, or constrictive pericarditis, it is called **acute benign pericarditis**.

• Sudden onset of **severe chest pain,** which increases by inspiration (differs from pain of myocardial ischemia) and may radiate to the abdomen. Pain decreases by changing from the supine position to sitting forward.
• Low grade **fever**.
• **Friction rub (to and fro) murmur**, which is **leathery** high-pitched scratchy sounds and increases in intensity with expiration. It is present throughout the cardiac cycle, making it possible to differentiate these from pleural rubs whose sounds are related to inspiration.
• **ECG:** Classically, the ECG changes associated with acute pericarditis evolve through 4 stages:
Stage I: diffuse ST segment elevation and PR segment depression.
Stage II: normalization of the ST and PR segments.
Stage III: widespread T wave inversion.
Stage IV: normalization of the T waves.
The ST elevation seen early is usually present in all leads, but in post-myocardial infarction pericarditis, the changes may be more localized. The diffuse distribution and the absence of reciprocal ST segment depression distinguish these changes from the ECG changes of myocardial infarction.
Depression of PR segment seen on the ECG reflects superficial injury of the atrial myocardium and may be the earliest sign of acute pericarditis on the ECG.

Treatment:

• Symptomatic treatment such as an analgesic.
• Salicylates such as aspirin or non-steroidal anti-inflammatory drugs such as ketorolac are the most commonly used to decrease pericardial inflammation.
• Corticosteroids can be used.
Elective surgery should be postponed for at least 6 weeks.

Chronic Constrictive Pericarditis

Pathology:

There is **fibrous scaring** and adhesions of both pericardial layers forming **a rigid shell around the heart** which:
• impedes (limits) diastolic filling of the heart. The heart will fill only to a fixed volume causing **decreased stroke volume and increased central venous pressure.**
• causes **equalization of diastolic pressures (as in cardiac tamponade).**

Causes:

The same as acute pericarditis.

Clinical Picture:

Chronic constrictive pericarditis **mimics right ventricular failure**.
1- Increased venous pressure (mainly on the right side) together with **right ventricular failure** leading to:

• Exaggerated distention of **neck veins (central venous pressure) during inspiration (Kussmaul's sign).** It is first described by Dr. Adolf Kussmaul in 1873. It occurs more often in patients with constrictive pericarditis than in those with cardiac tamponade.
• **Hepatic venous congestion** causing hepato-splenomegaly and ascites.
• Central venous pressure tracing will resemble that of right ventricular infarction due to prominent **"a" and "v" waves and steep "x" and "y" descents i.e., M or W configuration.** Often the steep "y" descent (dip) is short lived. A mid-diastolic plateau wave (h wave) occurs giving a **square root sign or Friedreich's sign** because diastolic blood flow from the atrium to the ventricle is initially rapid (steep y descent) then is abruptly stopped by the restrictive pericardial shell (plateau or h wave) (figure 25-27).
2- Atrial arrhythmias (atrial flutter or fibrillation) are common due to affection of the SA node by the disease process.
3- Conduction blocks.
4- Pulsus paradoxus: accentuated drops in systolic blood pressure (> 10 mm Hg) and pulse volume during inspiration. It is more common in cardiac tamponade and rare in constrictive pericarditis because the venous return does not increase during inspiration in constrictive pericarditis.
5- An early diastolic sound (pericardial knock) is often heard in patients with constrictive pericarditis, but not in cardiac tamponade.

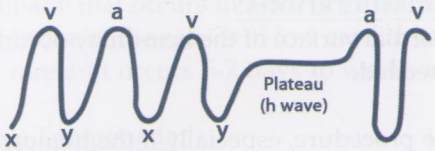


Figure 25-27: Central venous pressure with pericardial constriction

Investigations:

1- Chest x-ray: • A normal small (or large) heart.
• Calcium is seen in the pericardium (figure 25-28).

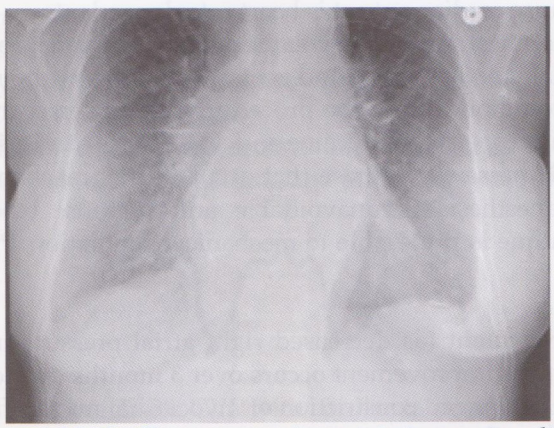


Figure 25-28: Chest x-ray of constrictive pericarditis

2- ECG: • Low-voltage QRS complexes.
• Inversion of T waves.
• Notched P waves.
• Arrhythmias and heart blocks.

3- CT scan, MRI, and trans-esophageal echocardiography are better in demonstrating pericardial thickening. Trans-esophageal echocardiography shows **ventricular discordance** (exaggerated increase in the right ventricular size with a reciprocal decrease in the left ventricular size during inspiration).

Differential Diagnosis

Differentiation between constrictive pericarditis and restrictive cardiomyopathy

	Constrictive Pericarditis	Restrictive Cardiomyopathy
Clinical Picture	• Previous history of pericarditis, cardiac surgery, trauma, radiotherapy, connective tissue disease. • Mitral or tricuspid regurgitation that is not usually present.	• Not present • Often present
Echo-cardiography	• Motion of mitral annulus: normal. • Respiratory variation in mitral and tricuspid flow velocity > 25% in most cases. • Ventricular septal movement with respiration: toward left ventricle on inspiration. • Equilibration of diastolic pressures in all cardiac chambers: within 5 mm Hg in nearly all cases. • Respiratory variation of ventricular peak systolic pressures: right and left ventricular peak systolic pressures are out of phase.	• Restricted. • < 15% in most cases. • Little toward left ventricle. • In only a small proportion of cases. • Right and left ventricular peak systolic pressures are in-phase.
MRI/CT	• Show pericardial thickening in most cases.	• Rarely shows pericardial thickening.
Endo-myocardial biopsy	• Normal or nonspecific	• Shows amyloid deposition in some cases.

Treatment:

Pericardectomy: Surgical removal of the constricting adherent pericardium via median sternotomy is usually done.

Anesthetic Problems and Considerations:

1- Massive bleeding from the epicardial surface of the heart may occur; so,
- A large bore venous access is needed.
- Blood transfusion is prepared.

2- CPB may be used to facilitate the procedure, especially if the **hemorrhage** is difficult to be controlled.

3- The pericardium is **generally dissected away from the left ventricle first** because dissection of the right ventricle first causes pulmonary edema.

4- Preoperative optimization of the **intravascular fluid volume is essential.**

5- In general, myocardial function is normal, but **some drugs** should be avoided that cause:
- **Excessive cardiac depression.**
- **Vasodilation and hypotension.**
- **Decreased heart rate** because cardiac output is heart rate dependent.

Therefore, opioids, benzodiazepines, small dose volatile agents, and pancuronium are preferred.

6- Monitoring: **Invasive** arterial blood pressure and central venous pressure measurements are needed.

7- Cardiac arrhythmias are common during the procedure due to direct mechanical stimulation of the heart; so, **anti-arrhythmic drugs** especially lidocaine and an electrical **defibrillator should be available.**

8- Elevations in intra-thoracic pressure as those that occur during mechanical ventilation can result in **profound hypotension**. If anesthesia is unavoidable and regional block is not possible, then a **spontaneous breathing technique is preferable** to mechanical ventilation. Preload should be maintained and tachycardia avoided.

9- Postoperatively:
- **The hemodynamic improvement** (as decreased right atrial pressure increases the cardiac output) does not occur immediately, but improvement **occurs over 3 months** due to:
  - Disuse atrophy from the prolonged constriction of myocardial muscle fibers.
  - The persistent constrictive effect from the sclerotic epicardium (visceral pericardium), which is not removed with the parietal pericardium.
- **Ventilatory insufficiency** may occur and need postoperative ventilation.
- **Pneumo-pericardium** may occur.

Pericardial Effusion

It is usually associated with acute pericarditis causing accumulation of the fluid in the pericardial sac.

Causes:

The same causes of acute and chronic pericarditis.

Clinical Picture:

a- Acute accumulation of fluid in the pericardial sac (even a small volume of 100-200 mL) increases the intra-pericardial pressure causing **cardiac tamponade** (see later).

b- Chronic accumulation of fluid causes stretch of the pericardium to accommodate the fluid up to large volumes (1000 mL), without significant increase in the intra-pericardial pressure.

Pericardial effusion only (without tamponade) may cause dyspnea.

Investigations:

1- Echocardiography (the most useful).

2- CT scan.

Cardiac Tamponade

Pathology:

- There is **accumulation of fluid (or blood)** in the pericardial sac **under pressure,** which increases the intra-pericardial pressure resulting in **impaired diastolic filling of the heart (i.e., diastolic dysfunction and not systolic dysfunction).** This decreases the stroke volume resulting in hypotension and low cardiac output syndrome and increases the central venous pressure.
- In absence of severe left ventricular dysfunction, equalization of the diastolic pressure occurs throughout the heart at **20 mm Hg** i.e., RAP = RVEDP = LAP = LVEDP = 20 mm Hg.

Causes:

The same as pericardial effusion, in addition to the following cause:
- **Postoperatively after cardiac surgery**; this is either:

- **Immediate acute** cardiac tamponade that occurs in 1-5% of patients. It occurs over minutes, hours, or after few days postoperatively. It is one of the causes of low cardiac output syndrome **(pump failure).**
- **Delayed** cardiac tamponade is rare and occurs 5-7 days to weeks after surgery especially in patients treated with anticoagulants.

N.B.: Regional or Loculated Cardiac Tamponade:

- It is less common. **Single chamber tamponade** can occur after surgery. Blood and **blood clots** distribute unevenly around the heart **compressing an individual chamber**. Postoperative right atrial hematoma often becomes localized to the anterior and lateral walls. Left atrial clots are more commonly found behind the left atrium where they become encysted in the posterior space in the oblique sinus.
- It is usually misdiagnosed because the classical features of tamponade are frequently absent.

Clinical Picture:

A high index of suspicion is necessary:

1- Increased central venous pressure causes:

- **Kussmaul's sign** (especially if associated with constrictive pericarditis).
- Central venous pressure (CVP) waves that show:
  - **normal or prominent x descent** due to increased systolic atrial filling.
  - **absent y descent,** due to impaired diastolic filling and atrial emptying (figure 25-29).

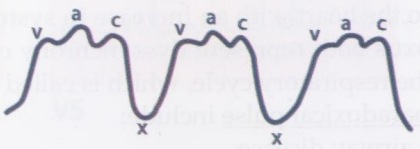


Figure 25-29: CVP with cardiac tamponade

2- Profound hypotension, which causes reflex activation of the sympathetic nervous system resulting in:

- Increased heart rate and peripheral vasoconstriction to maintain cardiac output (which is heart rate dependent).
- Tachypnea.

3- Muffled heart sounds.

N.B.: **Beck's triad** (= neck vein distention (increased CVP), muffled heart sounds, and hypotension,) is present in 30% of patients with acute cardiac tamponade.

Neck vein distension (increased CVP), muffled heart sounds, and ascites are another triad, which is present in patients with chronic cardiac tamponade.

4- Pulsus Paradoxus (Paradoxical Pulse):

It is an **accentuated drop in the systolic blood pressure (> 10 mm Hg)** and pulse volume during inspiration.

Explanation of pulsus paradoxus (and Kussmaul's sign):

- The right heart fills from blood entering the chest cavity due to a pressure gradient between the extrathoracic vasculature (superior and inferior vena cava systems) and intrathoracic chambers (the right atrium and right ventricle).

The left heart fills with blood moved by a pressure gradient between the intrathoracic, intrapulmonary vasculature (the pulmonary veins) and the intrathoracic, extrapulmonary left atrium and left ventricle.

- In **normal conditions**:
  - **During spontaneous inspiration,**
    - The venous return increases and **fills the right heart** smoothly without resistance due to increased negative intra-thoracic pressure (i.e., the extrathoracic to intrathoracic pressure gradient in increased) resulting in **more filling of the right ventricle and a decrease in CVP**.
    - **In the same time,** the capacity of **pulmonary** blood vessels increases due to **vasodilation** resulting in lung congestion and pooling of blood in the lung with **a decrease in filling of the left ventricle** and **a decrease in systolic blood pressure** (< 10 mm Hg).

    This means during normal spontaneous inspiration, there are a fall in the CVP (with more right ventricular filling) and a fall in systolic blood pressure (with less left ventricular filling).
  - **During expiration,**
    - The venous return decreases with decreased filling of the right heart due to increased intra-thoracic pressure resulting in **an increase in CVP**.

- The capacity of **pulmonary** blood vessels decreases due to **vasoconstriction** resulting in delivery of more blood from the lung to the left heart with **an increase in systolic blood pressure.**

- In **cardiac tamponade:**
  - During inspiration,
    - The venous return increases due to increased negative intra-thoracic pressure, but with **decreased filling of the right heart** (due to tamponade) resulting **in increased CVP (Kussmaul's sign)**.
    - The increase in venous return fills the right ventricle increasing right ventricular size causing **shift of the inter-ventricular septum towards the left ventricle**, with subsequent limiting filling of the left ventricle (due to restricted cardiac size by the tamponade) i.e., the right heart filling is done at the expense of the left heart. The capacity of **pulmonary** blood vessels increases due to **vasodilation** resulting in lung congestion and pooling of blood in the lung. Thus left ventricular preload, stroke volume, and **systolic blood pressure decrease more.**

  During mechanical ventilation, more restriction on the venous return occurs, worsening cardiac tamponade.
  - During expiration,
    - The venous return decreases due to the increased positive intra-thoracic pressure resulting in **a decrease in CVP.**
    - The capacity of **pulmonary** blood vessels decreases due to **vasoconstriction** resulting in delivery of more blood from the lung to the heart with **an increase in systolic blood pressure.**

Kussmaul's sign and pulsus paradoxus both represent dyssynchrony or opposing responses of the right and left ventricles to filling during the respiratory cycle, which is called **"ventricular discordance"**.

Other conditions associated with a paradoxical pulse include:

- Asthma and chronic obstructive airway disease.
- Airway obstruction.
- Pulmonary embolism.
- Ruptured diaphragm.
- Pneumothorax.

All these conditions are associated with a significant inspiratory decrease in the intra-pleural pressure. (figure 25-30).

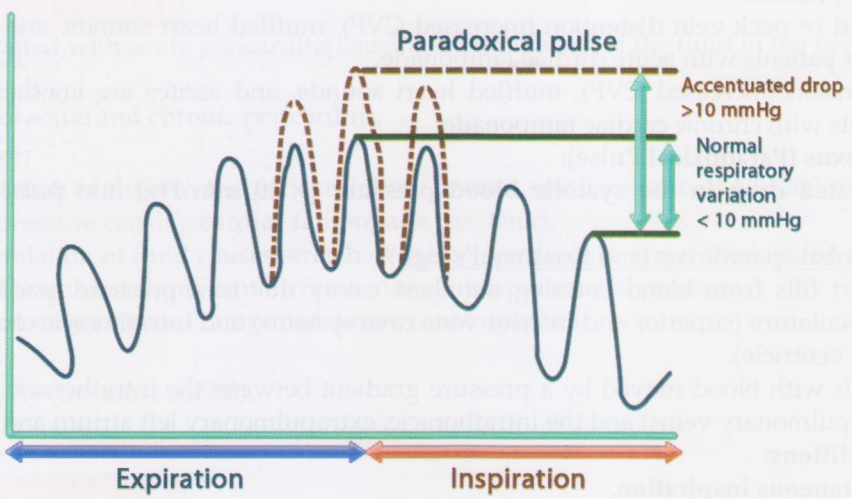


Figure 25-30: The paradoxical pulse

Investigations:

1- ECG:

- **Decreased voltage** due to a short circuit effect of the pericardial fluid.
- **Non-specific ST segment and T wave changes.**
- **Myocardial ischemia** if the increased trans-mural pressure on the ventricles interferes with the coronary blood flow.
- **Electrical alternans**: It is cyclic changes in the magnitude of the P wave, QRS complexes, and T wave, occurring in 10-15% of patients due to beat-to-beat oscillation of the heart within the fluid in the pericardial sac (figure 25-31).

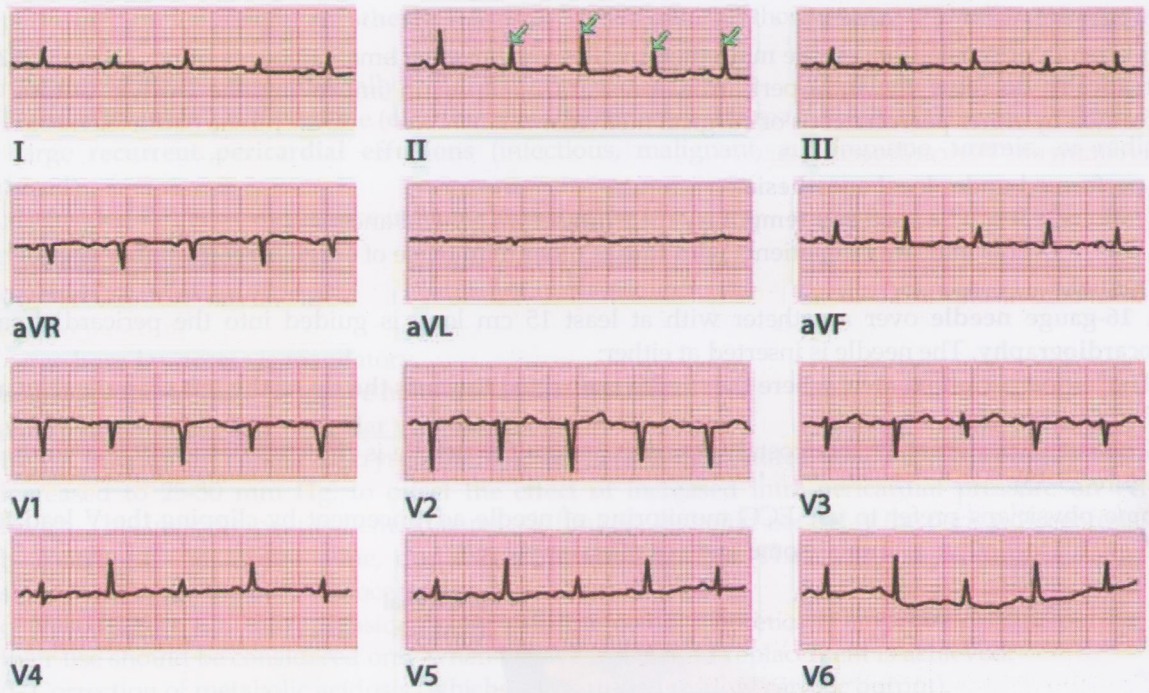


Figure 25-31: An ECG shows electrical alternans with low QRS complex voltage

2- Chest X-Ray: may show:

- Normal cardiac size **until 250 mL** of fluid is present in the pericardial sac.
- **Obscuration of the pulmonary vessels at the hilum**.
- A **globular or water bottle configuration** of the heart (figure 25-32).
- Clear lungs.
- Separation of epicardial and pericardial pads.

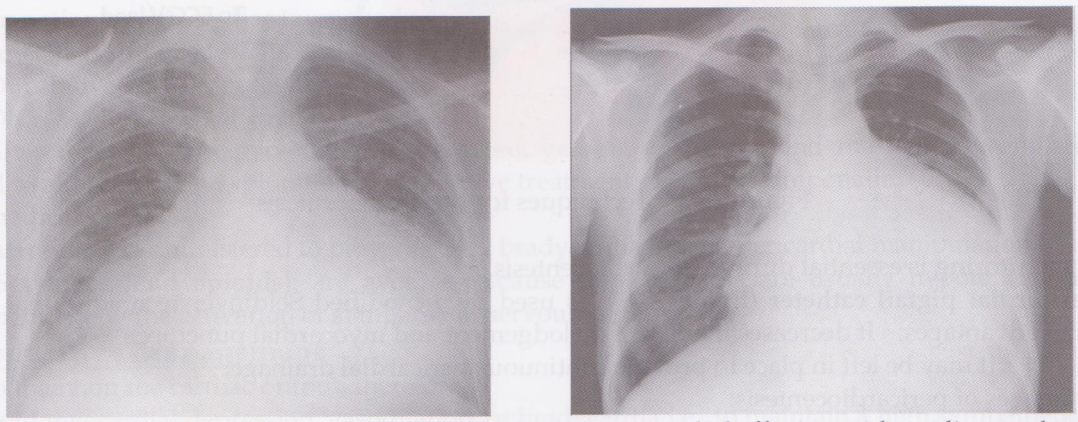


Figure 25-32: Two different patients with massive pericardial effusion with cardiomegaly. The heart appears flask shaped and the cardiac shadow cannot be seen through the effusion

3- Precordial and Trans-esophageal Echocardiography (the most accurate form of detection) may show:

- **Pericardial effusion** and its amount. Echocardiography can diagnose pericardial effusion as small as 20 mL.
- Echocardiography cannot always confirm cardiac tamponade, but signs of cardiac tamponade include:
  - **Diastolic compression or collapse of the right atrium and right ventricle** (i.e., diastolic inward wall motion).
  - **Leftward displacement of the ventricular septum during inspiration.**
  - **Exaggerated increase in the right ventricular size** with a reciprocal **decrease in the left ventricular size during inspiration (i.e., ventricular discordance)**.

▫ **Equilibration of pressures within the cardiac chambers.**

Treatment:

Drainage of pericardial fluid is the main therapy. Removal of even small amounts of pericardial fluid can dramatically decrease the intra-pericardial pressure resulting in improving the cardiac output. It is performed by either percutaneous or surgical methods:

a- Percutaneous Pericardiocentesis:

It is performed under **local anesthesia.**

Indications: • It can be used as a **temporary** measure before general anesthesia.
• It is indicated in patients with causes other than those of surgical removal (see later).

Technique:

• A **16-gauge needle** over a catheter with at least 15 cm long is guided into the pericardial sac by **echocardiography**. The needle is inserted at either:
▫ The left para-xiphoid area, where the needle is directed towards **the tip of the left scapula at an angle of 45 degrees** or
▫ The left para-sternal 4th intercostal approach, where the needle is directed perpendicular to the skin (figure 25-33).

• Some physicians prefer to use ECG monitoring of needle advancement by clipping the V lead to the needle. This technique is cumbersome and not often employed.

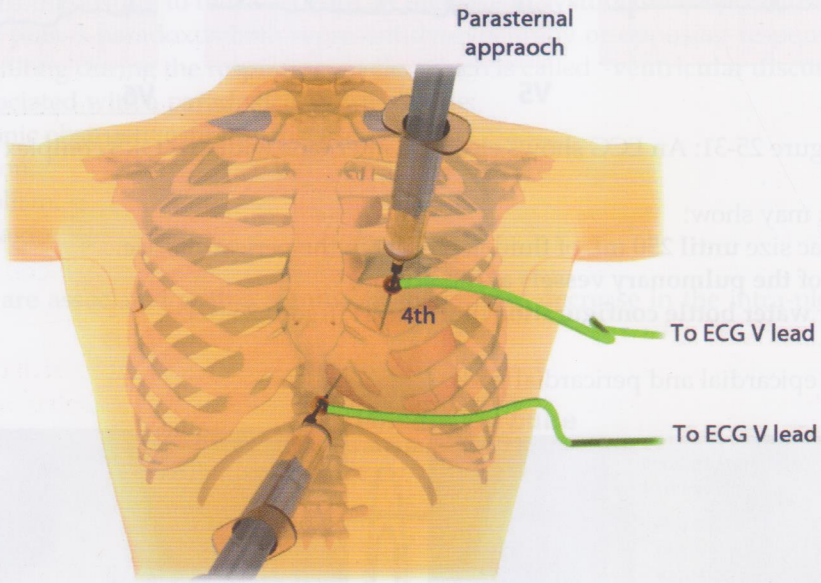


Figure 25-33: Techniques for pericardiocentesis

• **ECG monitoring** is essential during pericardiocentesis.

• **A pericardial pigtail catheter** (figure 25-34) is used by a modified Seldinger technique that has the following advantages: ▫ It decreases the risk of dislodgement and myocardial puncture.
▫ It may be left in place to provide continuous pericardial drainage.

Disadvantages of pericardiocentesis:

It may cause heart laceration, coronary injuries, arrhythmias, or pneumothorax.



Figure 25-34: A pigtail catheter

b- Surgical or Thoracoscopic Peri-cardiostomy:

It is performed under **general anesthesia.** It is done via left anterior thoracotomy or median sternotomy.

Indications:

It can be used for any cause especially:

- **Traumatic**: either postoperative (e.g., thoracotomy) or chest trauma.
- Large **recurrent pericardial effusions** (infectious, malignant, autoimmune, uremic, or radiation induced).

N.B.: Left sided thoracoscopy can be used for drainage.

Anesthetic Management

Preoperative Management

Patient Preparation

1- A large **bore i.v. access** is mandatory.

2- Temporary measures to improve hemodynamics include:

a- Expansion of the intravascular volume:

By i.v. infusion of colloid or crystalloid, 500 mL over 5-10 minutes until the right atrial pressure is increased to 25-30 mm Hg, to offset the effect of increased intra-pericardial pressure on venous return. This improvement in hemodynamics is limited. It should not delay the pericardiocentesis.

b- Inotropes: e.g., isoprenaline, dopamine, and dobutamine. They are also of limited value and should not delay the pericardiocentesis.

c- Vasodilators e.g., nitroprusside or hydralazine could theoretically improve cardiac output, but their use should be considered only when intravascular fluid replacement is achieved.

d- Correction of metabolic acidosis (which occurs due to the low cardiac output).

As increased H^+ ions further depresses myocardial contractility and attenuates the positive inotropic effect of inotropes. It is treated by $NaHCO_3$ 0.5-1 mEq/kg i.v.

e- Atropine:

it is administered to treat bradycardia, which in turn increases the cardiac output (cardiac output is heart rate dependent). Bradycardia occurs due to vagal reflexes from the increased intra-pericardial pressure.

3- Pericardiocentesis:

It should be preformed under local anesthesia (with/without ketamine sedation) before general anesthesia is administered because **general anesthesia can cause severe hypotension and even cardiac arrest in patients with cardiac tamponade** due to:

- Anesthetic induced peripheral vasodilation.
- Direct myocardial depression.
- Decreased venous return.

Then after the hemodynamic status is improved, general anesthesia and mechanical ventilation are applied to allow surgical exploration for definitive treatment of cardiac tamponade.

4- Premedications:

- **Atropine**: is administered to prevent reflex bradycardia during pericardial manipulation.
- **Sedatives (and opioids):** are avoided because these patients are usually hypotensive and are dependent on the activation of sympathetic nervous system.

Intraoperative Management

Aim: to maintain the cardiac output; therefore,

- Avoid myocardial depression, vasodilation, or bradycardia i.e., to maintain a high sympathetic tone.
- Avoid increased intra-thoracic pressure e.g., coughing, straining, and mechanical ventilation.

Monitoring:

Besides the standard monitors, invasive blood pressure and central venous pressure monitoring are essential.

Induction and Maintenance:

- **Ketamine:** for induction and maintenance.

It is **a drug of choice** because it increases myocardial contractility, systemic vascular resistance, and heart rate due to: ▫ direct central sympathetic stimulation.

▫ inhibition of norepinephrine uptake into post-ganglionic sympathetic nerve endings.

N.B.: Ketamine in patients with a high sympathetic tone already produces intrinsic myocardial depression, which decreases the cardiac output and arterial blood pressure.

• **Benzodiazepines** e.g., diazepam for induction and N_2O for maintenance.
• Muscle relaxants: **Pancuronium** is the drug of choice.
• After intubation and **before drainage, hand ventilation with slight decrease in the minute ventilation is done** i.e., avoid vigorous mechanical ventilation until the drainage is done because mechanical ventilation further decreases the venous return. **After drainage, mechanical ventilation** can be applied.
N.B.: Awake intubation and spontaneous ventilation are theoretically desirable, but coughing, straining, hypoxemia, and especially acidosis should be avoided.

Intraoperative Fluid: should be **generous** to maintain venous return.

Intraoperative Complications:

1- Severe Hypotension and Circulatory Collapse may occur after induction.
It is treated by: • I.v. infusion of **inotropes** e.g., isoproterenol, dopamine, dobutamine, or a small dose of i.v. epinephrine (10 mg).
• Personnel and equipment should be prepared to perform an **emergency pericardiocentesis,** if circulatory collapse persists.

2- Intraoperative Hypertension may occur after relief of a severe tamponade due to increased left ventricular stroke volume, hypervolemia, inotropes, vasopressors, and inadequate anesthesia.
It is treated by: ▫ increasing the depth of anesthesia and
▫ vasodilators e.g., Na nitroprusside.

3- Complications due to Surgery:

• Severe hemorrhage.
• **Disruption of aorto-coronary or internal mammary artery grafts** with subsequent **ischemia.**
• Disruption of **valve prosthesis,** especially in the mitral position, if the heart is raised out of the pericardial cavity.
• **Arrhythmias** during heart manipulations.
• **An un-drained retro-sternal hematoma** may increase the risk of infection.

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THORACIC SURGERY

26

- Physiological aspects during thoracic anesthesia:
  Lateral decubitus position
  Open pneumothorax
  One-lung ventilation
- Anesthesia for thoracotomy
- Anesthesia for tracheal resection
- Anesthesia for thoracic telescopic procedures:
  Thoracoscopy (video-assisted thoracoscopy)
  Bronchoscopy (fiberoptic and rigid)
  Mediastinoscopy
  Esophagoscopy (fiberoptic and rigid)
- Lung transplantation
- Lung volume reduction surgery
- Anesthesia for a patient with a transplanted lung

Physiological Aspects during Thoracic Anesthesia

Three events affect thoracic anesthesia:

- Lateral decubitus position.
- Open pneumothorax.
- One lung ventilation.

A) Lateral Decubitus Position

In the Awake State (with Spontaneous Breathing):

There is **ventilation/perfusion matching** (figure 26-1) because:

- The lower dependent lung receives **more perfusion** (about 60%) due to the effect of **gravity** while the upper nondependent lung receives about 40% of the total blood flow.
- The lower dependent lung receives also **more ventilation** because the contraction of the dependent hemi-diaphragm is more efficient because the dependent diaphragm assumes a higher position in the chest by the abdominal contents (compared to the upper hemi-diaphragm, which disproportionately shares in supporting the weight of abdominal contents). Therefore, the dependent lung is on a more favorable part of the compliance curve.

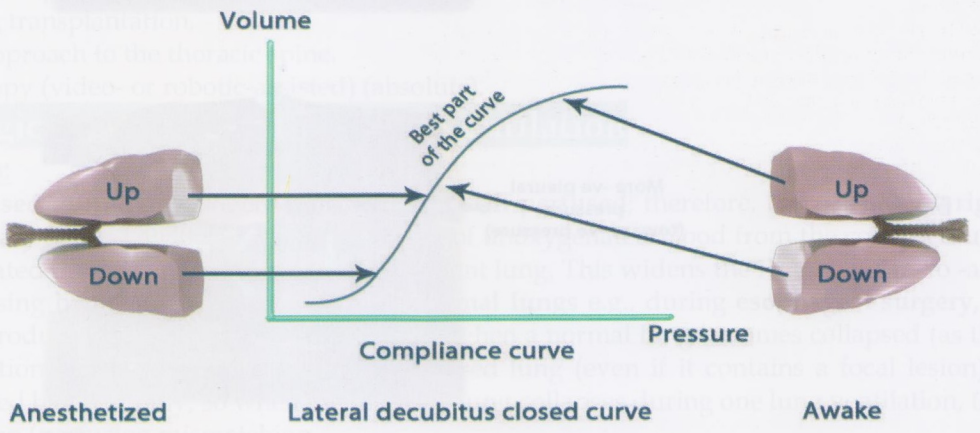


Figure 22-1: Lung compliance during lateral decubitus position

During General Anesthesia:

On Spontaneous Ventilation:

There is ventilation/perfusion mismatching in the dependent lung because:

- Perfusion is increased due to the effect of gravity, but
- Ventilation is decreased due to the following reasons:

- **Anesthesia decreases the functional residual capacity (FRC)** moving the upper lung to a more favorable part of the compliance curve, but moving the lower lung to a less compliant position.
- The **dependent chest wall is constricted** by the operating room **table**, and lateral movement is limited by **the bolsters or bean-bags** used to hold the patient in position.
- The increase in intra-abdominal pressure that occurs with general anesthesia, decreases diaphragmatic movements.
- **Opening the nondependent side of the chest** further increases the differences in compliance between the two sides, because the upper lung now is less restricted in movement.

Therefore, the upper lung is ventilated more than the lower lung which has greater perfusion.

On Positive Pressure Ventilation:

There is **further ventilation/perfusion mismatching** because of the above causes in addition to:

- **Mechanical ventilation** produces more ventilation in the upper lung because it is more compliant than the lower one.
- **Muscle paralysis** allows the abdominal contents to rise up further against the dependent hemi-diaphragm producing further more ventilation in the upper lung and less ventilation in the lower lung.

B) Open Pneumothorax (Opening of the Chest)

Normally the lungs are kept expanded by a negative pleural pressure (the net result of the tendency of the lung to collapse and the chest wall to expand).

Opening one side of the chest (or after chest trauma) causes **loss of the negative pleural pressure;** so, the elastic recoil of the lung on that side, causes lung **collapse,** with subsequent mediastinal shift and paradoxical respiration (figure 26-2). On spontaneous ventilation, progressive hypoxemia and hypercarbia occur.

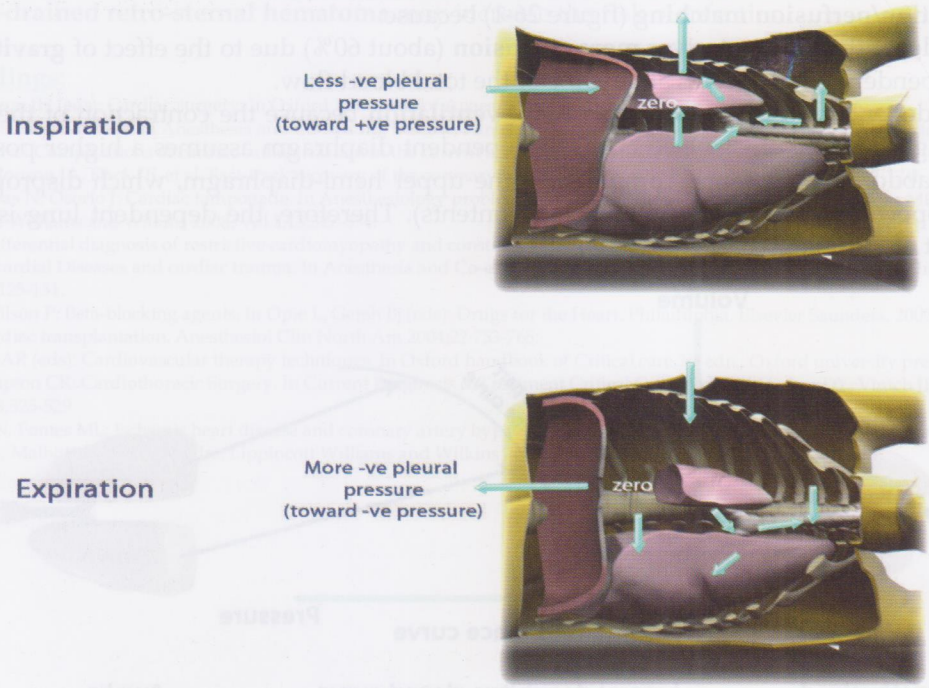


Figure 26-2: Effect of open pneumothorax on the respiration

1) Mediastinal Shift:

During spontaneous ventilation in the lateral position,

- **Expiration** makes the pleural pressure less negative (i.e., towards the positive side) on the dependent side, but not on the open side (which is at a pressure of zero atmosphere) producing **upward shift of the mediastinum.**
- **Inspiration** makes the pleural pressure more negative (i.e., towards the negative side) on the dependent side, but not on the open side (which is at a pressure of zero atmosphere) producing **downward shift of the mediastinum.**

This shift decreases the contribution of the dependent lung to the tidal volume.

2) Paradoxical Respiration:

During spontaneous ventilation in the lateral position, to- and fro- gas flow between the dependent and nondependent lung takes place.

- **Expiration** decreases the pneumothorax and allows the gas to flow from the dependent to the upper lung across the carina. This produces **outward movement of the rib cage.**
- **Inspiration** increases the pneumothorax and allows the gas to flow from the upper lung to the dependent lung across the carina. This produces **inward movement of the rib cage.**

Therefore, pendulum breathing is produced.

General anesthesia with mechanical ventilation should be applied to overcome these effects, as mechanical ventilation produces inflation of the dependent and nondependent lung, decreasing the pneumothorax and increasing chest inflation during inspiration.

C) One Lung Ventilation (OLV) or One Lung Separation

It is sometimes called "Lung Deflation Techniques". During lung surgery, the more diseased lung is the one which will be uppermost and collapsed i.e., one-lung ventilation.

Indication

a) Patient-related: They are mostly **absolute indications**.

- To **isolate the other lung**: ▫ To confine infection to one lung e.g., bronchiectasis or lung abscess.
  ▫ To confine bleeding to one lung.
- To **separate ventilation** of each lung: ▫ Broncho-pleural fistula
  ▫ Tracheo-bronchial disruption.
  ▫ Large lung cyst or bulla.
  ▫ Surgical procedures on major conducting airway.
  ▫ Unilateral broncho-pulmonary lavage (pulmonary alveolar proteinosis)
- Severe hypoxemia due to **unilateral lung disease**.

b) Procedure-related: to facilitate the surgical exposure. They are mostly **relative indications** except thoracoscopy, which is an absolute indication.

- Repair of thoracic aortic aneurysm.
- Lung resection e.g., pneumonectomy, lobectomy, segmental resection.
- Esophageal surgery.
- Mediastinal exposure.
- Single lung transplantation.
- Anterior approach to the thoracic spine.
- Thoracoscopy (video- or robotic-assisted) (absolute).

Physiological Effects of One Lung Ventilation

a) Hypoxia:

- **The collapsed lung is no longer ventilated, but still perfused**; therefore, there is a **large right-to-left intrapulmonary shunt (20-40%)** leading to mixing of unoxygenated blood from the collapsed upper lung with oxygenated blood from the ventilated dependent lung. This widens the P_{A-a} (alveolar- to -arterial) O_2 gradient causing hypoxemia. **In patients with normal lungs** e.g., during **esophageal surgery,** one lung ventilation produces **a greater level of hypoxemia** when a normal lung becomes collapsed (as this causes more ventilation/perfusion mismatching). A diseased lung (even if it contains a focal lesion) tends to have a reduced blood supply, so when the diseased lung collapses during one lung ventilation, this causes less ventilation/perfusion mismatching.
- Normally, **during two-lung ventilation in upright and supine positions**, the **right lung** receives approximately **55%** of the total blood flow, whereas the **left lung** receives the remaining **45%**. Gravity causes a vertical gradient in the distribution of blood flow in the lateral decubitus. Therefore, blood flow to the dependent lung is significantly greater than that to the nondependent lung. When the **right lung is nondependent**, it receives **45%** of the total blood flow, whereas **55%** perfuses the **dependent left lung**. When **the left lung is nondependent**, it receives **35%** of the total blood flow, whereas the **dependent right lung** receives **65%**. Therefore, the average blood flow of the nondependent lung is approximately 40% of the total blood flow, whereas the dependent lung is perfused with the remaining 60%.

During single lung ventilation, the hypoxic pulmonary vasoconstriction reflex (HPV reflex) should decrease the blood flow to the non-dependent lung by 50%. Therefore, the nondependent lung should be

able to decrease its blood flow from 40% to 20% of the total blood flow, and the nondependent/dependent lung blood flow ratio should be 20%: 80%.

• If there was no shunt during two-lung ventilation conditions (ignoring the normal 1-3% shunt flow due to the bronchial, pleural, and thebesian vessels), then we would expect the ideal total shunt single-lung ventilation to be a minimal of 20% of the total blood flow. PaO_2 (with FiO_2 = 1.0) should be about 280 mmHg if hemodynamic and metabolic states are normal. Clinically, the PaO_2 (when FiO_2 = 1.0) ranges from 150-250 mmHg.

Blood flow to the upper non-ventilated lung is decreased by the following factors:

1- **Hypoxic pulmonary vasoconstriction reflex (HPV reflex).** This is the main cause, where deprivation of the upper nondependent lung from oxygenation stimulates the HPV reflex, but usually it does not occur to a significant extent in the first few hours after lung collapse.

2- **Pathological condition** of the upper nondependent lung (if it is diseased and will be resected) will initiate **more HPV reflex**; therefore, there will be more hypoxia if the upper nondependent lung is normal and collapsed due to surgical related indication to facilitate surgical exposure.

3- **Surgical compression of the upper lung by retractors.**

b) Hypercarbia:

It **does not occur** usually with OLV because there are:

- a decrease in the dead space/tidal volume ratio increasing CO_2 excretion and
- an increase in the intrapulmonary shunt decreasing CO_2 excretion.

Therefore, the net effect is **unchanged CO_2** elimination provided that, the minute ventilation and tidal volume are unchanged and there is no preexisting CO_2 retention.

Techniques of One Lung Ventilation (OLV)

OLV can be performed by one of the following techniques:

- A double-lumen endobronchial tube.
- A single-lumen endotracheal tube with a bronchial blocker.
- A single-lumen endobronchial tube.

A) Double-Lumen Endobronchial Tube (DLT)

Advantages:

It is the most commonly used due to:

- Its relative **ease** of placement.
- The ability of **ventilating either one or both lungs.**
- The ability of **suctioning either one or both lungs.**

Types:

There are disposable plastic (polyvinyl chloride) DLTs and red rubber DLTs. Disposable plastic DLTs are easier to insert and less likely to damage tracheo-bronchial structures than red rubber DLTs. Disposable DLTs are more flexible and have more compliant cuffs with an improved internal to external lumen diameter relationship.

Name	Bronchus intubated	Carinal hook	Shape of Lumen
Robert-Shaw	Right or left	No	D-shaped
Carlens	Left	Yes	Oval
White	Right	Yes	Oval
Bryce-Smith	Left	No	Round
Bryce-Smith & Salt	Right	No	Round

Robert-Shaw Tube:

It is the most common type used especially the **disposable** left-sided version.

It is available in different sizes. It is available either disposable or reusable (figure 26-3).

French Gauge	Internal Diameter	Uses
26 (recently available)		Children > 30 kg body weight or > 8-10 years of age
28 (recently available)		Older children
32 (recently available)		Older children
35	5.0 mm	a short female
37	5.5 mm	a tall female
39	6.0 mm	a short male
41	6.5 mm	a short male

The French gauge is explained in more details in the appendix of this book.

Silbroncho Double-Lumen Tube:

It is a left DLT with a very flexible, wire-reinforced tip. Its tip allows easy passage through the pharynx and larynx, unlike the ordinary DLTs, which pass through the larynx with more difficulty (figure 26-4).

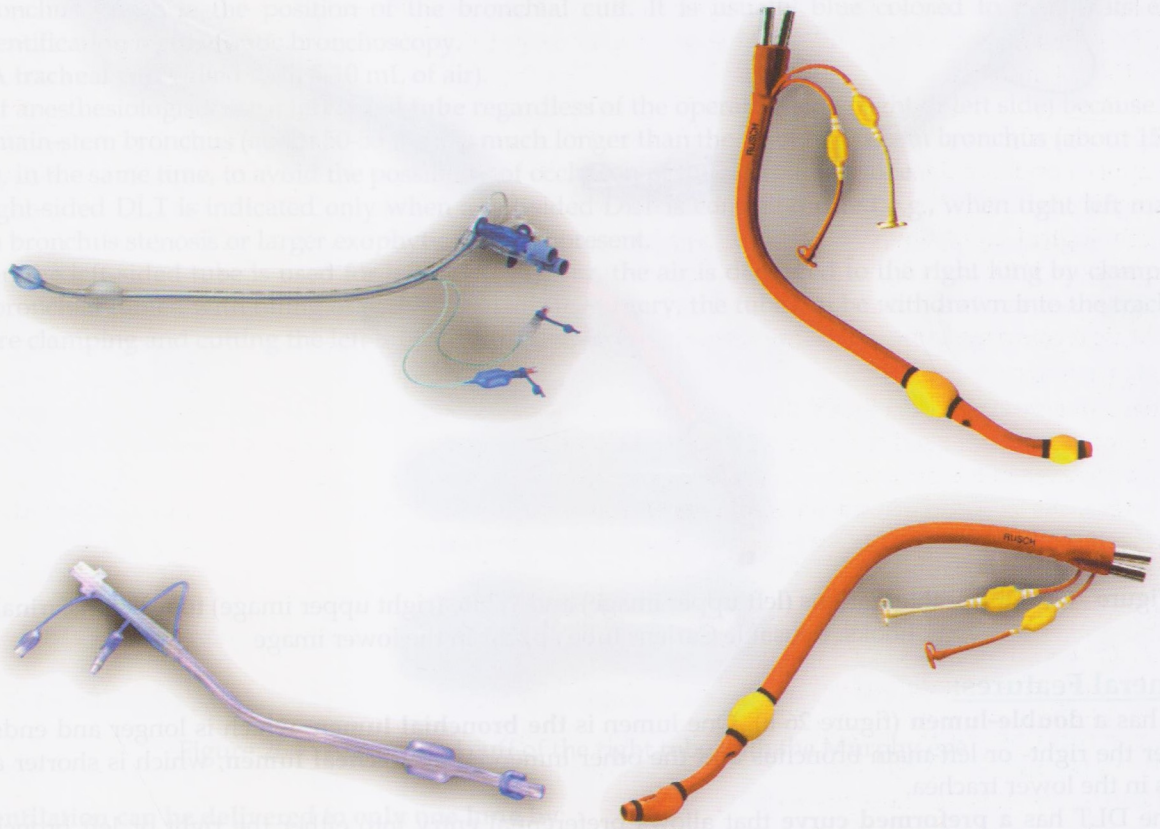


Figure 26-3: Robert-Shaw tubes; disposable and reusable left-sided tubes (above) and disposable and reusable right-sided tubes (below)

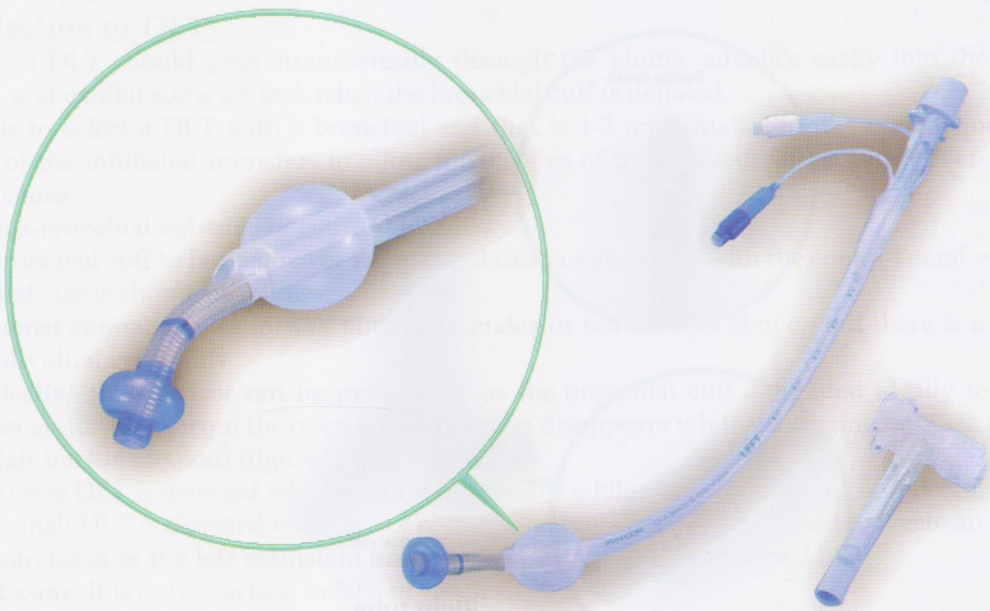


Figure 26-4: A Silbroncho tube

Carlens and White tubes with carinal hooks appear in the figure 26-5.

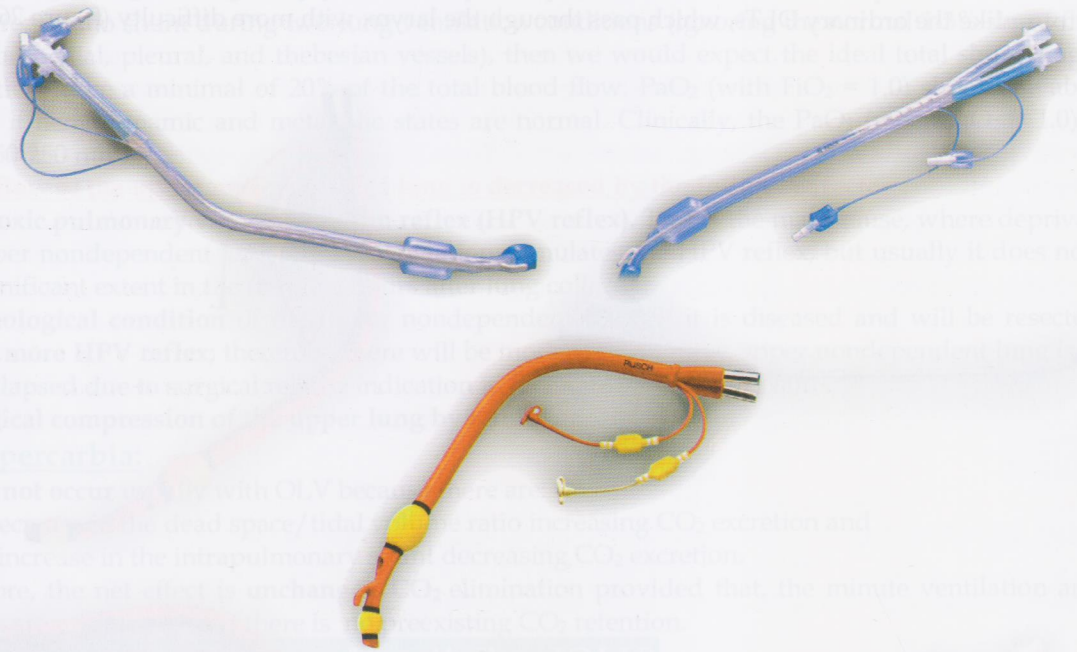


Figure 26-5: Disposable Carlens (left upper image) and White (right upper image) tubes with carinal hooks. Reusable Carlens tube appear in the lower image

General Features:

- It has a **double-lumen** (figure 26-6). One lumen is **the bronchial lumen**, which is longer and ends in either the right- or left-main bronchus and the other lumen is **the tracheal lumen**, which is shorter and ends in the lower trachea.
- The DLT has **a preformed curve** that allows preferential entry into either the right or left bronchus where:
  - **Right-sided tubes** are designed for **left thoracotomies** (to ventilate the right lung and collapse the left lung).
  - **Left-sided tubes** are designed for **right thoracotomies** or are used when **non-pulmonary surgery is undertaken.**

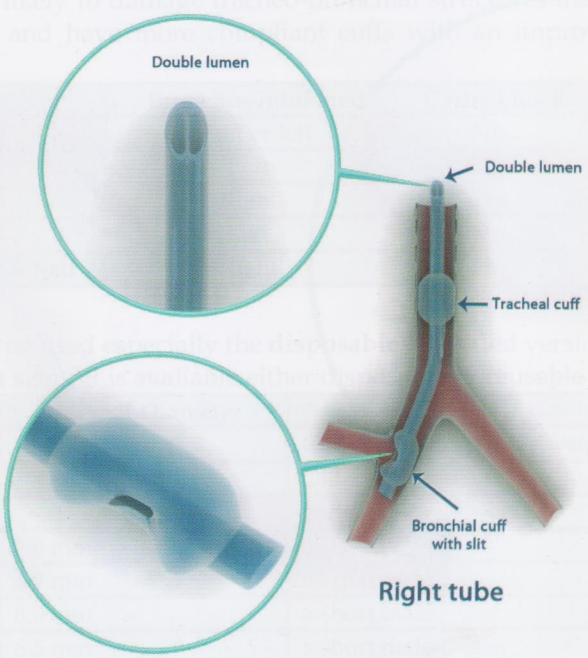


Figure 26-6: Position of a right DLT

- A DLT has **two cuffs**:
  - **A bronchial cuff** (filled with 1-2 mL of air). The right sided endobronchial tubes have **a doughnut-shaped cuff, which has a slit in the bronchial cuff** (a Murphy eye) (figure 26-7) for ventilating the right upper lobe because the right upper lobe bronchus takes an origin usually 0.5-1.0 cm from the right main bronchus which is the position of the bronchial cuff. It is usually blue colored to permit its easy identification by fiberoptic bronchoscopy.
  - **A tracheal cuff** (filled with 5-10 mL of air).

Most anesthesiologists use a **left sided tube** regardless of the operative side (right or left side) because the left main-stem bronchus (about 50-55 mm) is much longer than the right main-stem bronchus (about 15-20 mm), in the same time, to avoid the possibility of occlusion of the right upper lobe.

A right-sided DLT is indicated only when a left-sided DLT is contraindicated e.g., when tight left main-stem bronchus stenosis or larger exophytic lesion is present.

When the left-sided tube is used for left-sided surgery, the air is delivered to the right lung by clamping the bronchial lumen with filling of both cuffs. During surgery, the tube can be withdrawn into the trachea before clamping and cutting the left bronchus if necessary.



Figure 26-7: A bronchial cuff of the right tube with the Murphy eye

- **Ventilation can be delivered to only one lung by**:
  - **clamping** either the bronchial or tracheal lumen with inflation of both cuffs and
  - opening the port on the connector of one lumen to allow the ipsilateral lung to collapse while the other lumen is used for ventilation of the other lung.

Some tubes have a **carinal hook** e.g., Carlens and White (modified Carlens), but this hook produces some difficulties on passing them through the larynx; so, some clinicians do not prefer them.

Size Selection of DLT:

Generally, a DLT should pass atraumatically through the glottis, advance easily into the trachea and bronchus, and exhibit some air leak when the bronchial cuff is deflated.

The aim is to select a DLT with a bronchial end that is 1-2 mm smaller in its outer diameter than the diameter of the intubated bronchus to allow for the size of the inflated cuff, because over-inflation and over-size cause:

- Trachea-bronchial ischemia or rupture.
- The bronchial cuff to herniate over the tracheal carina interfering with the contra-lateral ventilation.

The selected size is chosen as follows:

1- The most common sizes for **tall and short males or female**s (as above), but there is a considerable inter-individual variability.

2- Clinically, air leak test can be performed; as the bronchial cuff is inflated ideally to the point at which an audible leak from the open tracheal lumen disappears while ventilating only via the bronchial lumen (air bubble method) (figure 26-8).

- A too large DLT is detected when no air leak is heard while the bronchial cuff is deflated.
- A too small DLT is detected when > 3 cc of air in the bronchial cuff is needed to create an air seal.

3- Measurement of the left mainstem bronchus diameter can be performed by:

- **Chest x-ray:** It is only practical in 50% of cases.
- **Chest CT or three-dimensional CT scan reconstruction**.

4- Measurement of the tracheal diameter at the level of the clavicle and calculation of the left mainstem bronchus diameter can be performed by:

- **Chest x-ray**: The tracheal diameter and left mainstem bronchus ratio is 0.68.
- **Chest CT or three-dimensional CT scan reconstruction**: The ratio is 0.75 for men and 0.77 for women.

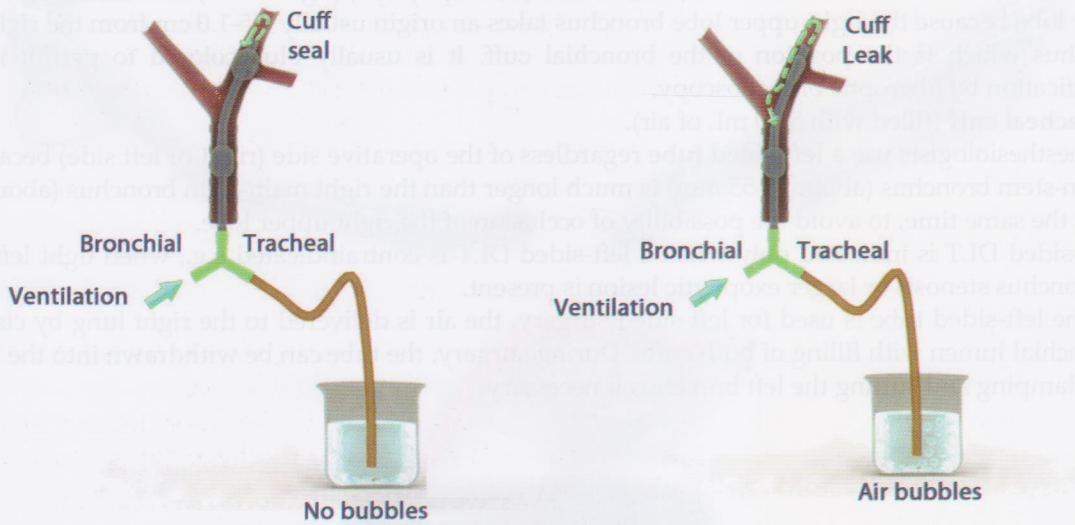


Figure 26-8: Air bubble method

Placement of the DLT:

- Laryngoscopy with **a curved (Macintosh) blade** usually provides a better visualization than a straight blade (the straight blade may be more useful if the larynx is anterior).
- The DLT is passed with **the distal curvature concave anteriorly** and **is rotated 90 degrees (toward the side of the bronchus to be intubated) as the tip enters the larynx,** so that the distal curve is angled towards the intended bronchus. The DLT is **advanced until resistance** is felt. The average depth of insertion is about 29 cm (from the teeth).
- If the DLT placement is difficult, intubate the patient with a smaller (6.0-7.0 ID) regular tube, then this regular tube is exchanged for the DLT by utilizing **a specially designed catheter guide (tube exchanger)**. An approach for OLV in a patient with difficult intubation is discussed later.

Confirmation of Proper Tube Placement:

Confirmation of the tube placement should be done immediately **after tube placement** and **after the patient is positioned** for surgery because the tube may move, relative to the carina, as the patient is turned into the lateral decubitus position.

Confirmation is done by:

a) A preset Protocol: (e.g., for left-sided tubes).

1- Inflate the **tracheal cuff** (5-10 mL of air).

2- Check for **bilateral breath sounds**. Unilateral breath sounds indicate that the tube is too far down (i.e., the tracheal opening is endobronchial).

3- Inflate the **bronchial cuff** (1-2 mL of air).

4- **Clamp the tracheal lumen.**

5- **Check for unilateral left sided breath sounds**.

- Persistence of right-sided breath sounds indicates that the bronchial opening is still in the trachea (i.e., the tube should be advanced).
- Unilateral right-sided breath sounds indicate incorrect entry of the tube into the right bronchus.
- Absence of breath sounds over the entire right lung and the left upper lobe indicates the tube is too low in the left bronchus.

6- Unclamp the tracheal lumen and **clamp the bronchial lumen.**

7- Check for **unilateral right breath sounds**. Absence or decreased breath sounds indicate that the tube is still not far enough down and the bronchial cuff is occluding the distal trachea.

b) Flexible Fiberoptic Bronchoscopy:

It is the most accurate method. Most double-lumen tubes easily accommodate bronchoscopes with a 3.6-4.2 mm outer diameter. When the bronchoscope is introduced into the tracheal lumen and advanced to the tracheal orifice, the following structures can be seen:

- The **carina** should be **visible**.
- **The bronchial tip of the tube** should be seen **entering the left bronchus** (and not in one of the lobar bronchi).
- **The top of the bronchial cuff** (usually colored blue) should be **visible**, but should not extend above the carina. If the bronchial cuff of a left sided double-lumen tube is not visible, it may be too low, enough to obstruct the orifice of the left upper lobe; so, the tube should be withdrawn until the cuff becomes visible.

Mal-positioning of Double Lumen Tubes:

Mal-positioning of a DLT is indicated by:

- poor lung compliance and
- low exhaled tidal volume.

Mal-positioning of a DLT can be one of the following conditions:

1) The tube is too deep:

It usually occurs on using a small tube in a tall individual. The bronchial cuff can obstruct the left upper lobe orifice and the opening of the tracheal lumen may lie within the left bronchus.

In some cases, it is possible that the bronchial cuff lies, too deep, below the left upper lobe orifice with the opening of tracheal lumen still remaining above the carina. This situation is suggested by collapse of only the left lower lobe when the bronchial lumen is clamped.

2) The tube is not deep enough:

The bronchial lumen is still in the trachea or the bronchial cuff occludes the right bronchus.

For (1) and (2), deflation of the bronchial cuff improves ventilation of the affected lung and helps in identifying the problem.

3) The Tube inadvertently enters the wrong bronchus.

In this case, the fiberoptic bronchoscope can be used to reposition it into the correct side as the bronchoscope is passed through the bronchial lumen to the tip of the tube. Under direct vision, the tube and the bronchoscope are withdrawn together into the trachea just above the carina. The bronchoscope alone is then advanced into the correct bronchus. The DLT is gently advanced over the bronchoscope, which functions as a stylet to guide it into the correct bronchus.

Complications of DLTs:

1- Hypoxemia due to tube misplacement or occlusion.

2- Traumatic laryngitis (especially with tubes that have a **carinal hook**).

3- Tracheo-bronchial rupture or lacerations only due to over-inflation of the bronchial cuff.

4- Inadvertent suturing of the tube to a bronchus during surgery (it is detected by difficulty in withdrawing the tube at extubation).

Contraindications of DLTs:

1- Patients with a lesion (e.g., airway stricture, endo-luminal tumors) that is present somewhere along the pathway of the tube and thus could be traumatized.

2- Unsuitable DLT size e.g., very young patients.

3- Patients with upper airway anatomy that precludes safe tube insertion e.g., recessed jaw.

4- Extremely critically ill patients who have a single lumen tube already in place and who cannot tolerate cessation of mechanical ventilation and positive end-expiratory pressure (PEEP) for a short period while the DLT is being inserted.

Under these conditions, OLV can be achieved by another technique such as endobronchial blocker or a long uncut endotracheal tube placed into a mainstem bronchus.

B) Single-Lumen Endotracheal Tube with a Bronchial Blocker

Bronchial blockers are inflatable devices, which are passed alongside or through a single-lumen endotracheal tube (i.e., coaxially), to selectively occlude a bronchial orifice. They include:

- Univent tube.
- Uniblocker.
- Arndt endobronchial blocker (wire-guided or snare-guided endobronchial blocker).
- Cohen flexitip endobronchial blocker.
- Rüsch bronchial blocker
- Inflatable Catheter.

Advantages of Bronchial Blockers:

- **Simple** to use.
- Can be used in **adults and pediatrics** even less than 30 kg body weight because they are single lumen-tubes.
- Can be used to produce OLV in a patient **with a difficult airway.**
- Can be used **when there are contraindications to DLTs.**
- Can be used **in emergent conditions** because it can be applied via the already existing single-lumen endotracheal tube.
- A channel within the blocker (except in the inflatable catheters) **allows the lung to deflate** (though slowly) and can be used for **suctioning or insufflating oxygen**.
- **No need to change the endotracheal tube at the end of the surgery** when a patient needs postoperative ventilation.

Disadvantages of Bronchial Blockers: (in comparison to DLTs).

- **Inability to suction efficiently or intermittently ventilate the lung** distal to the blocker without deflating the balloon especially when an inflatable catheter is applied.
- The endobronchial blockers should be placed under direct visualization with the guidance of a rigid or flexible fiberoptic **bronchoscope** or direct transthoracic manipulation by a skilled surgeon.
- Difficulty in maintaining position in **the right mainstem bronchus** to isolate the right upper lobe efficiently if the takeoff is close to carina.
- **Easily slipped** resulting in life-threatening obstruction of the trachea if the bronchial blocker dislodges proximally
- **Bilateral lung ventilation** if the cuff is not inflated properly.
- **Inadvertent suturing of the tube to a bronchus during surgery** (it is detected by difficulty in withdrawing the tube at extubation).
- The cuffs of some blockers have **a high-pressure low volume**, thus may exert excessive pressure on the bronchial wall.

1) A Univent Tube

It is a single lumen-endotracheal tube **with a built-in side channel** (2 mm internal diameter) for a retractable bronchial blocker. The rigid internal blocker facilitates tracheal intubation because, when retracted within the tube, it acts like a stylet, angling the tip of the tube for laryngeal passage. It is available in several sizes from **3.5-9.0 mm internal diameter.** The smallest size 3.5 internal diameter has an external diameter of 6 mm, which can be used in **a child more than one year of age.** It is rarely used nowadays, but may be used in **emergency conditions such as pulmonary hemorrhage**. It has a hexagonal grip, which enhances ability to rotate the blocker from outside the tube (figure 26-9).

A **TCB univent tube** (torque-controlled blocker "TCB") is recently developed. It is made of silicon, which allows for full rotation of the blocker cuff into the selected bronchus. It is easier to be manipulated than the previous nylon catheter.



Figure 26-9: A univent tube

Technique:

- A univent tube is inserted in the trachea as the standard endotracheal tube.
- The tube is placed with the blocker fully retracted; its natural curve is directed such that:
  - turning the tube with the curve concave towards the right preferentially directs the bronchial blocker towards the right bronchus.
  - turning the tube such that the curve is concave to the left usually directs the blocker towards the left bronchus.
- The bronchial blocker **must be** advanced, positioned, and inflated **under direct vision via a flexible bronchoscope.** The bronchoscope passes via an adaptor with a self- sealing diaphragm, which allows uninterrupted ventilation.
- The cuff of the blocker is a **high pressure-low volume cuff;** so, the minimum volume that prevents a leak should be used. It is usually inflated with 6-7 mL air.

2) Uniblocker

Uniblocker is the blocker of the univent tube, which is now available as an independent blocker to be inserted through a standard endotracheal tube. It is blue in color with a stylet and angled tip with elliptical or spherical balloon. Its central lumen can be capped or used for suction/O_2 insufflation. It can be used coaxially or in parallel with the endotracheal tube. It has an external hexagonal piece near the proximal end of the endobronchial blocker that makes it easier to rotate during placement. **TCB uniblocker** is a new version called **torque- controlled blocker (TCB)** that allows for full rotation of the blocker cuff (figure 26-10).

3) Coopdech Blocker

It is a bronchial blocker, similar to the uniblocker. It can be inserted inside an ordinary single lumen endotracheal tube (figure 26-11).

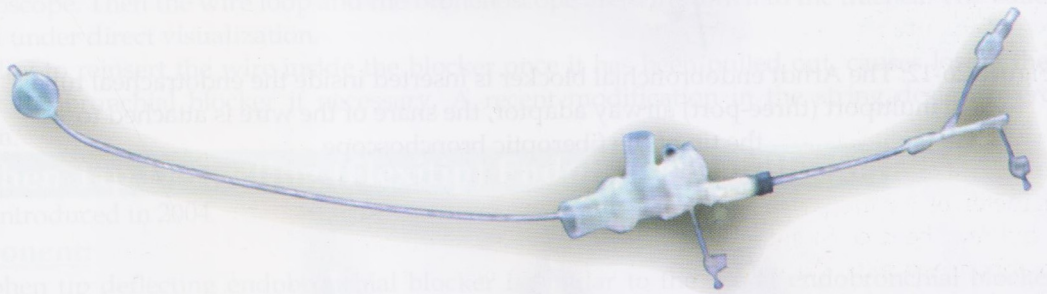


Figure 26-10: A uniblocker



Figure 26-11: A Coopdech blocker

4) The Arndt Endobronchial Blocker (Wire-guided or Snare-guided endobronchial blocker "WEB")

It has recently been developed by George Arndt in 1994, but with high cost (figure 26-12 and 26-13).

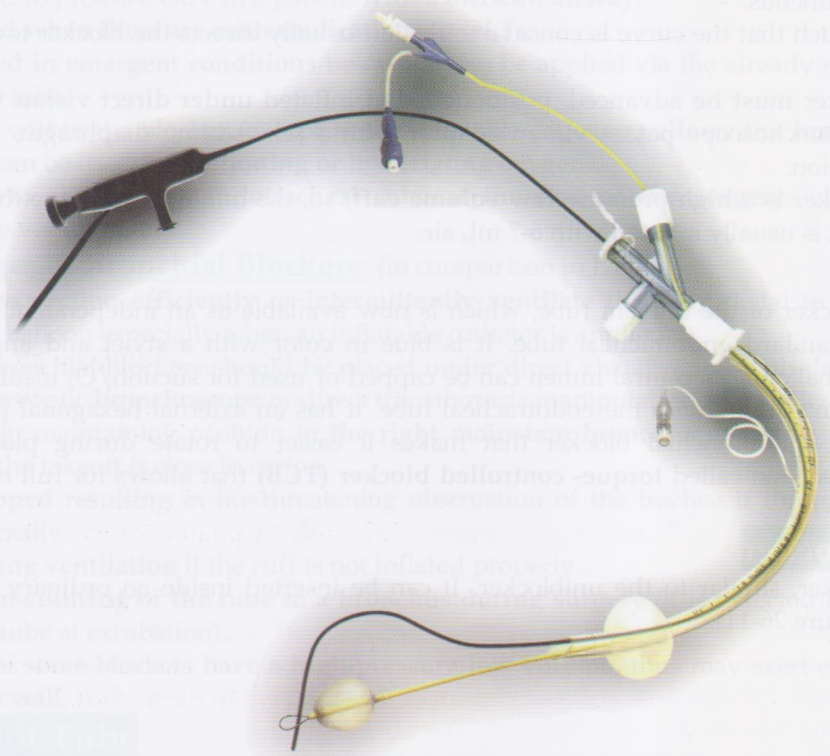


Figure 26-12: The Arndt endobronchial blocker is inserted inside the endotracheal tube via a multiport (three-port) airway adaptor, the snare of the wire is attached to the tip of the fiberoptic bronchoscope

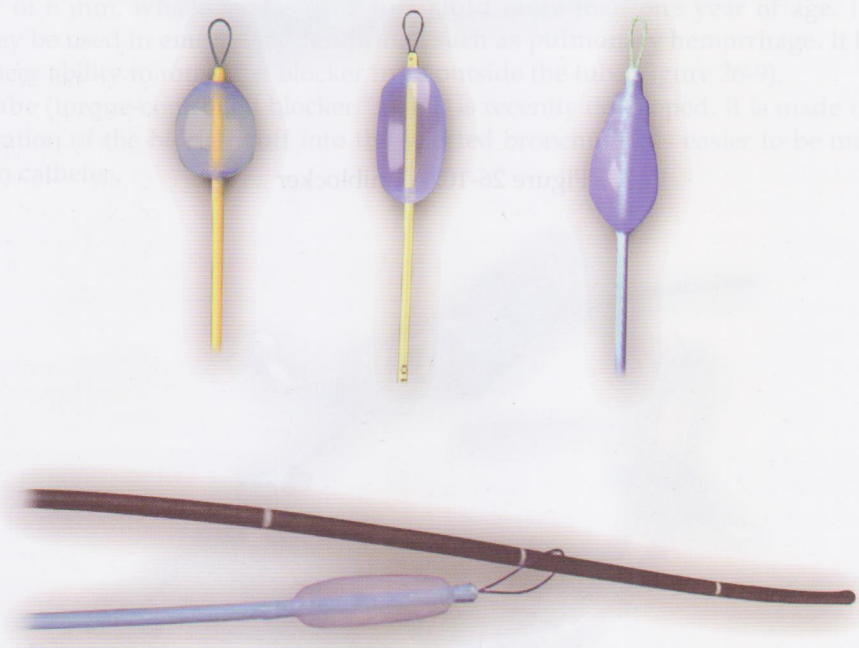


Figure 26-13: Different shapes of Arndt cuffs; spherical, elliptical, and pear shapes. The lower image shows the snare attached to the tip of fiberoptic bronchoscope

Component:

It is a latex-free yellow colored blocker with a blue inflatable balloon. It has a central lumen (1.4-1.8 mm) through which a guidewire with a looped end has been passed. The lumen is used to insufflate O_2 or suction after the wire loop is removed. It comes with a special adaptor that has four ports:

- A 15 mm endotracheal tube connector.
- A ventilation port to be connected to the anesthesia circuit.
- A bronchial blocker port that has a self-sealing diaphragm that also can be tightened around the blocker to keep it in place.
- A port for the bronchoscope.

It has a blue inflatable balloon, spherical, elliptical, or pear shaped, and a high-volume, low-pressure cuff. The elliptical shape makes it less likely to be dislodged and provides a longer sealing profile for the main bronchus.

Three sizes are available:

- 9 F (the smallest single lumen tube used with it is 7.5 mm ID); spherical (filled with 8 mL air) or elliptical (filled with 12 mL air) cuff.
- 7 F (the smallest single lumen tube used with it is 6.0 mm ID); spherical cuff (filled with 6 mL air).
- 5 F (the smallest single lumen tube used with it is 4.5 mm ID); spherical cuff (filled with 2 mL air).

These above sizes are available in pediatric (50-65 cm) and adult (65-78 cm) lengths.

Technique:

- Once the patient's trachea is intubated with a single lumen endotracheal tube, the three-way adaptor can be connected and ventilation started. Then the blocker with its guidewire (string) can be passed through its port inside the single lumen tube i.e., coaxially.
- The bronchoscope is passed through its port inside the single lumen tube, within the wire loop of the blocker and then advanced to the position to be blocked.
- After the desired location in the bronchial tree has been reached, the blocker is advanced over the bronchoscope. Then the wire loop and the bronchoscope are withdrawn to the trachea. The balloon is then inflated under direct visualization.
- Inability to reinsert the wire inside the blocker once it has been pulled out, causes losing the ability to redirect the bronchial blocker if necessary. A recent modification in the string design overcomes the problem.

5) Cohen Tip Deflecting (Flexitip) Endobronchial Blocker

It was introduced in 2004.

Component:

- A Cohen tip deflecting endobronchial blocker is similar to the Arndt endobronchial blocker. It has a spherical balloon. Its catheter is colored green, with side depth markings and side holes between the soft hollow tip and the balloon for evacuation of distal lung gas or insufflation of O_2 during use.
- A proximal control wheel that can be operated with the thumb and forefinger adjusts tip deflection during insertion. A large black arrow along one side of catheter just above balloon points at tip to identify direction of tip angulation, allowing endoscopist to line arrow up with desired direction of deflection before advancing and flexing the catheter into the appropriate bronchus.
- It is available in one size 9 F with 65 cm length.

Technique:

- It is inserted coaxial or parallel to a standard endotracheal tube with a small 4.0 mm fiberoptic bronchoscope. It uses a flexible soft tip that can be deflected to more than 90 degrees and easily directed into the desired bronchus to be blocked. The deflection of the tip is achieved by rotation of a wheel that is located at the proximal part of the bronchial blocker (figure 26-14).
- The blocker cuff is a high-volume, low-pressure balloon with a spherical shape that provides adequate seal of the bronchus.
- The lumen of the blocker is 1.6 mm that allows:
  - suction of the lung to facilitate deflation,
  - limited suction of the secretions and insufflation of oxygen to the collapsed lung in case of hypoxia.

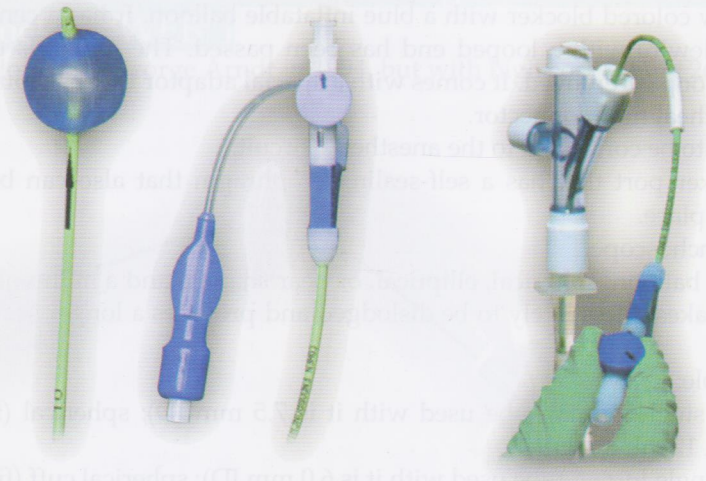


Figure 26-14: The Cohen tip deflecting endobronchial blocker (middle image) with its balloon (the left image) and Cook multiport adaptor while the Cohen blocker is inserted (the right image)

6) An Inflatable Catheter

such as: ▫ **a Fogarty embolectomy catheter,**
▫ **a Foley urological catheter** (figure 26-15),
▫ **a Swan-Ganz catheter,**
▫ **a Magill balloon-tipped luminal blocker, or**
▫ **an atrio-septostomy catheter.**

It can be used as a bronchial blocker in conjunction with a regular endotracheal tube (inside or alongside); a guidewire in the catheter can be curved to facilitate the placement. Placement of these catheters requires direct guidance, with a flexible bronchoscope
It has many disadvantages; therefore, it is rarely used (see above).

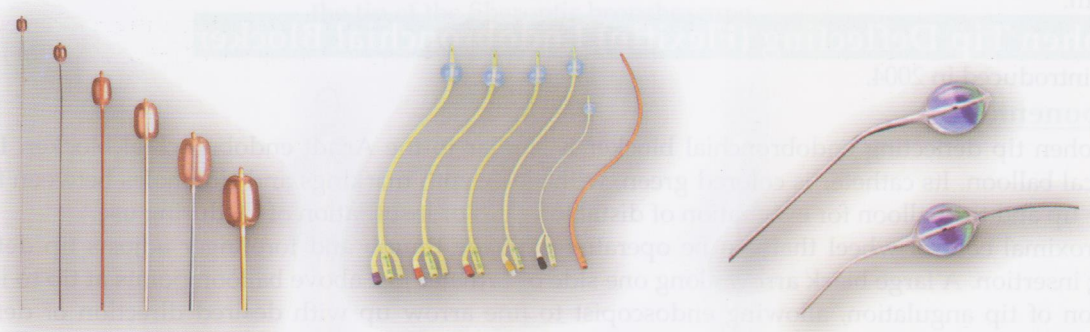


Figure 26-15: Fogarty catheters (left), Foley catheters (middle), and atrio-septostomy (right) catheters

C) Single-Lumen Endobronchial Tube

It is rarely used nowadays. It is used only in **emergency cases e.g., unilateral pulmonary hemorrhage**.

Types:

1) Gordon-Green tube:

• It is **right-sided** single lumen tube for left thoracotomies as it is easily advanced to the right bronchus (figure 26-16). It has both **tracheal and bronchial cuffs** and a carinal hook. Inflating the bronchial cuff isolates and allows ventilation of only the right lung, while inflating the tracheal cuff (with deflating the bronchial cuff) allows ventilation of both lungs (although unequally).
• It has a much **larger slit** in the bronchial cuff (compared to right-sided double lumen tubes), leading to a high success rate in ventilating the right upper lobe.

Disadvantages:

• Risks of a carinal hook.
• Inability to suction the left lung.

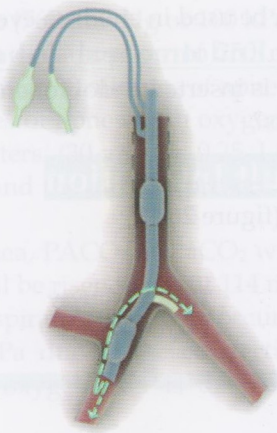


Figure 26-16: Gordon–green tube

2) Ordinary Uncut Single-Lumen Endotracheal Tube:

- It has the same size as that used for tracheal intubation (in infant, a smaller size by 1 mm ID is used).
- The tube can usually be advanced blindly into the right bronchus if the source of the hemorrhage is the left lung, but usually the right upper lobe is not ventilated.
- The tube is difficult to be advanced blindly into the left bronchus if the source of the hemorrhage is the right lung. This can be achieved by advancing the tube with its convexity posteriorly, while turning the head to the right. If this is not possible, it must be guided by bronchoscopy.

OLV in a Patient with a Tracheostomy

There are three options:

1- Double Lumen Tube or Univent Tube:

- It can be introduced through the tracheostomy stoma (like oro-tracheal tube), although these tubes are not specifically designed for this use.
- Depending upon the details of the patient's anatomy such as stromal diameter, distance between the skin and the anterior tracheal wall, and stroma-to-carinal distance, DLTs and Univent tubes may be difficult to place and position atraumatically and precisely.

2- Bronchial Blockers:

They are introduced either coaxially or alongside a single lumen tube or tracheostomy tube through the stoma or through the mouth.

3- Single Lumen Tubes:

They are inserted blindly or fiberoptically through the stoma.

OLV in Pediatrics

This can be achieved by one of the following methods:

A) Small Double Lumen Endobronchial Tubes (DLTs):

The smallest size available is 26 F gauge, which can be used for:

- Children > 30 kg body weight.
- Children > 8-10 years of age.

Disadvantages:

- With a narrow tracheal lumen, the small DLT does not allow the use of a pediatric fiberoptic bronchoscope to confirm correct placement.
- At the end of the operation, it must be exchanged with a single lumen tube if the child is left intubated.

B) Single Lumen Endotracheal Tube with a Bronchial Blocker:

1- Univent Tube:

It is as that of the adult type. It is available in sizes from 3.5 to 9.0 mm internal diameter. The smallest one can be used in **a child 1 year old**.

2- Fogarty Embolectomy catheter, Swan-Ganz catheter or atrio-septostomy catheter can be used in children and **infants.**

3- The Arndt Endobronchial blocker can be used in children even **in infants.**

C) Ordinary Uncut Single-Lumen Endotracheal Tube:

A smaller size by 1 mm ID is used, which is inserted endobronchially. It can be used **in infants.**

Q: How can OLV can be applied in infants?

OLV in a Patient with Difficult Intubation

The following approach can be followed (figure 26-17):

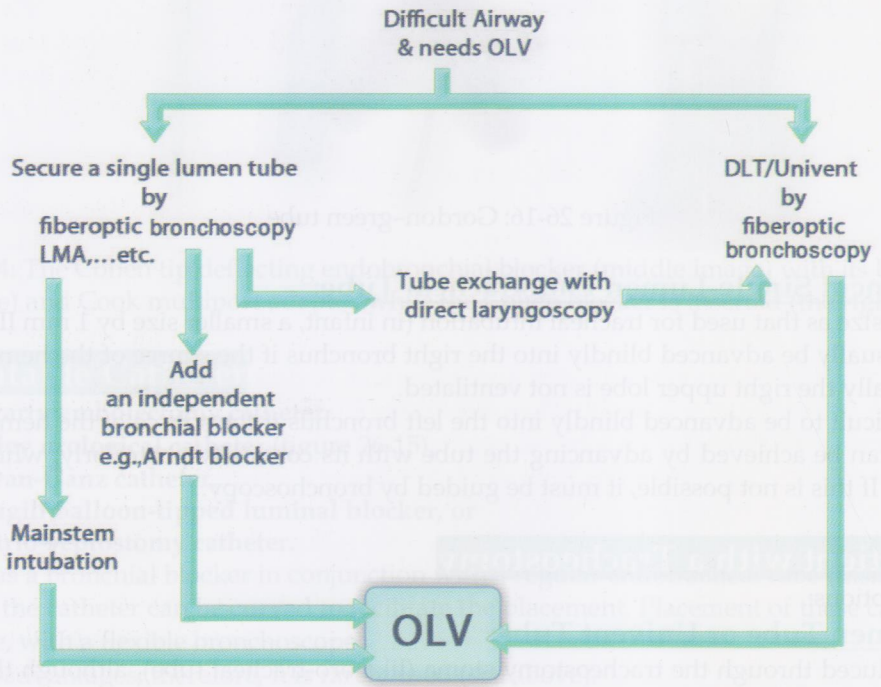


Figure 26-17: Approach to OLV in patients with a difficult airway:

Alternatives to OLV

A) Apneic Oxygenation (Diffusion Respiration):

It is first described by Draper and Whitehead in 1944.

Definition:

Ventilation is stopped for short periods while 100% O_2 is insufflated via an endotracheal tube at a rate > O_2 consumption. This allows oxygenation without lung expansion or interference with surgery.

Mechanism:

Apnea Whilst Breathing Air:

- At the onset of apnea. the oxygen available to support vital organ function is the summation of oxygen in the alveoli (about 200 mL) and oxygen combined with hemoglobin (about 800 mL) i.e., total 1000 mL. As oxygen consumption is 250 mL/min; therefore, after 2 min, the consumed oxygen is 500 mL (250 mL x 2) and the alveolar (PAO_2) and arterial (PaO_2) partial pressure of oxygen will be 28.8 mmHg (3.8 kPa). Within 4 min, severe hypoxemia (PAO_2 is < 3.8 mm Hg or 0.5 kPa) occurs resulting in cardiac arrest.
- Although the production of CO_2 is 200 mL/min, the addition of CO_2 to the alveolar air is rising slowly during periods of apnea because most of the produced CO_2 will be buffered in the body and only a small amount reaches the alveoli and remains in the blood. The alveolar ($PACO_2$) and arterial ($PaCO_2$) partial pressure of CO_2 at 2 minutes of apnea are 50 mm Hg (6.6 kPa). Within 4 min, $PACO_2$ increases to 54.7 mmHg (7.2 kPa), which is unimportant clinically.

Apnea Whilst Breathing 100% Oxygen:

- After breathing 100% oxygen, the gas composition in the alveoli will be:
  89% oxygen (676.4 mm Hg or 89 kPa), which is 2.4 liters,
  5% CO_2 (38 mm Hg or 5 kPa),
  6% water vapor (45.6 mm Hg or 6 kPa).

The total alveolar pressure is 1 atmosphere (760 mm Hg or 100 kPa).

- After 2 minutes of apnea with oxygen consumption of 250 mL/min, the PAO_2 and PaO_2 will only decrease to 664.24 mm Hg (87.4 kPa) and after 30 minutes of apnea, the PAO_2 and PaO_2 will only decrease to 600.4 mm Hg (79 kPa). After 30 minutes of apnea with oxygen consumption of 250 mL/min, the total oxygen consumption will be about 8 liters (30 min x 0.25 Liter). The difference between the total consumed O_2 in the 30 minutes (8 liters) and the already present in the alveoli (2.4 liters) is derived from the convection flow (see later).
- In the same time; after 2 minutes of apnea, $PACO_2$ or $PaCO_2$ will be risen to about 50 mm Hg (6.6 kPa) and after 30 minutes, $PACO_2$ or $PaCO_2$ will be risen to about 114 mmHg (15 kPa)
- Therefore, after 30 minutes, severe respiratory acidosis occurs ($PaCO_2$ is 114 mm Hg), but without hypoxia (PaO_2 is 600.4 mm Hg or 79 kPa due to the convective flow). Therefore, the only limit for continuation of oxygenation by apneic oxygenation is development of hypercarbia and respiratory acidosis.

Buffering the pH change with intravenous tri-hydroxymethyl-amino-methane (THAM) will extend the time of survival by using apneic oxygenation, but sodium bicarbonate is ineffective because it increases production of CO_2 during apnea.

Convective Flow:

- During normal ventilation, CO_2 diffuses from the blood to the alveoli at a rate of 200 mL/min. However, during periods of apnea, most of CO_2 produced is buffered within the body and only about 5-20 mL/min enters the alveoli.
- In the same time, 250 mL/min of O_2 continues to be absorbed from the alveoli to the blood i.e., the same rate during ventilation and apnea.
- This produces a net loss of volume and a fall in pressure inside the alveoli. This pressure drop causes **vacuum,** which makes convective gas flow or mass movement (not diffusion) from the airways to the alveoli provided the **patient's airway remains patent** and connected to an O_2 supply then O_2 will be passively drawn down the airway at a rate of about 245 mL/min.
- If the airway is obstructed, no gas will flow into the alveoli. In the same time, the oxygen inside the alveoli will be absorbed and lung volume will decrease by a rate of 245 mL/min resulting in alveolar collapse (i.e., absorption atelectasis). 1/3 of the alveolar volume will be lost within 2-3 minutes. This will cause intrapulmonary shunting and arterial hypoxemia. The shunt will increase above 50% in 2-3 minutes (figure 26-18).

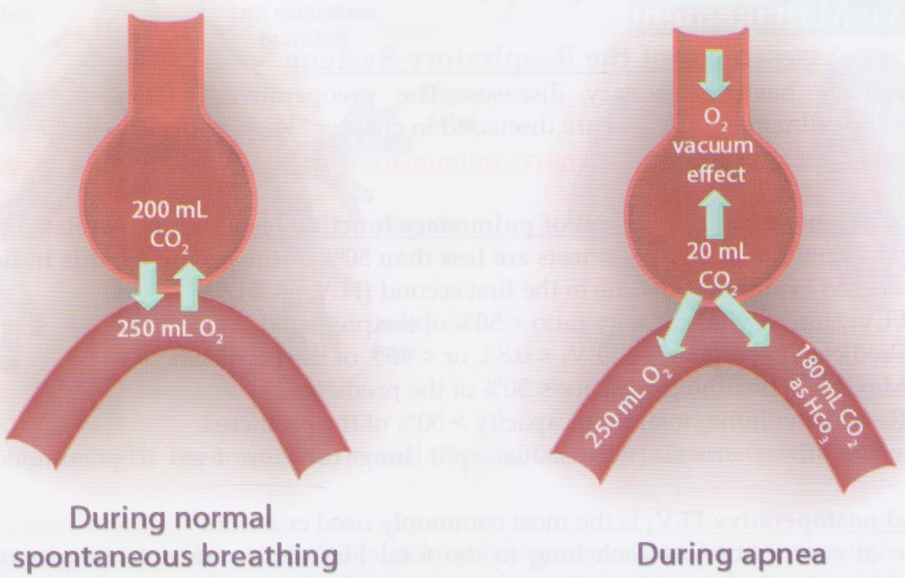


Figure 26-18: Apneic oxygenation

Clinical Applications:

- Apneic oxygenation can be used as an alternative to OLV because oxygenation can be maintained for about 20-30 minutes.

• **In suffocation** (airway obstruction), **gross hypoxia** occurs **after 90 sec** if the patient has been breathing air.

If the **patient is breathing air** and **no has obstruction** of airway as in intubating patients without preoxygenation, the patient develops gross hypoxia **after 2 min**.

With **preoxygenation for 3 minutes**, gross hypoxia occurs **after 6 minutes (up to 10-20 min)** in **normal weight patients** and **after 3 minutes** in **morbidly obese** patients.

• **During induction of anesthesia** while the patient is apneic and disconnected from the oxygen source for example, if the face mask is removed to permit laryngoscopy, room air will be drawn instead of O_2 down the trachea at same rate of about 245 mL/min. In about 30 seconds, nitrogen will start to enter the alveoli which are perfused (dependent) since the rate of extraction of oxygen from an alveolus is determined by its perfusion. Oxygen will be rapidly diluted in these alveoli and the time to significant hypoxemia may now be as little as 2-3 minutes. This is still substantially better than if the patient has not been preoxygenated at all.

	Periods of Apnea (Minutes)					
	0	2	4	15	30	60
After breathing air						
PAO_2 or PaO_2 (mm Hg)	90	28.88	< 3.8	Unsurvival		
$PACO_2$ or $PaCO_2$ (mm Hg)	38	50	54.7	Unsurvival		
After breathing 100% O_2						
PAO_2 or PaO_2 (mm Hg)	676.4	664.24	659.68	634.6	600.4	532
$PACO_2$ or $PaCO_2$ (mm Hg)	38	50	54.7	79.8	114	182.4

B) High Frequency Positive Pressure Ventilation.

C) High Frequency Jet Pressure Ventilation.

In both high frequency positive pressure and jet ventilation, a standard endotracheal tube is used with small tidal volumes (< 2 mL/kg). This decreases lung excursion and facilitates the surgery, as mediastinal bounce (to- and fro- movement) may interfere with the surgery.

Anesthesia for Thoracotomy

For example, lung resection.

Preoperative Management

1) Preoperative Assessment of the Respiratory System:

Majority of patients have pulmonary diseases. The preoperative assessment, preparations, and management of the pulmonary diseases are discussed in chapter "Respiratory Disease".

Prediction of operative risks and postoperative pulmonary complications after lung resection:

a) Preoperative Pulmonary Function Tests:

• **The degree of preoperative impairment of pulmonary function tests** is directly related to the operative risk. If preoperative pulmonary function tests **are less than 50% of the predicted, this indicates high-risk patients** e.g., ▫ Forced expiratory volume in the first second (FEV_1) < 2 L.

- ▫ FEV_1/forced vital capacity ratio < 50% of the predicted.
- ▫ Predicted postoperative FEV_1 < 0.8 L or < 40% of the predicted.
- ▫ Maximum breathing capacity < 50% of the predicted.
- ▫ Residual volume/total lung capacity > 50% of the predicted.

Presence of any of these criteria necessitates split lung function tests if pneumonectomy is still contemplated.

• **The predicted postoperative FEV_1** is the most commonly used criterion.

The percentage of contribution of each lung to the total FEV_1 is assumed to be proportionate to the percentage of the total pulmonary blood flow it receives as determined by radio-isotopic scanning (^{133}Xe or ^{99}Tc).

Predicted postoperative FEV_1 **= the % of blood flow to the remaining lung x total FEV_1.**

▫ If the **predicted postoperative FEV_1 is > 800 mL**, this indicates that **the remaining lung after pneumonectomy has a great effect on ventilation** while the diseased lung (to be removed) has a little effect on ventilation (i.e., the diseased lung is not well ventilated but perfused). Actually, removal of the

diseased lung will improve oxygenation by diverting its blood flow to the ventilated remaining lung. Therefore, the predicted postoperative FEV_1 (whole-lung FEV_1) > 800 mL after surgery is the amount a patient requires to avoid being dependent on mechanical ventilation.

- If the **predicted postoperative FEV_1 is < 800 mL,** but resection is still considered, **the ability of the remaining pulmonary vasculature to tolerate total blood flow can be tested** but is rarely done i.e., the diseased lung receives high blood flow and has a great effect on ventilation.

The main pulmonary artery on the diseased side is occluded with a balloon catheter; if the mean pulmonary artery pressure exceeds 40 mm Hg or PaO_2 decreases to < 45 mm Hg, the patient is not a candidate for pneumonectomy.

- **Predicted postoperative lung function may be calculated using lung segments.**

From a total of 19 segments, 3 in the upper lobes, 2 in both the middle lobe and lingula and 4 in the left and 5 in the right lower lobes. The fraction of lung remaining is multiplied by the preoperative spirometry measurement.

$$\text{Predicted postoperative } FEV_1 = \text{preoperative } FEV_1 \times (1-(\text{resected segments}/19))$$

Using whole-lung spirometry to predict postoperative lung function may be invalidated if the regional function of the lung is not known. For example, a patient with a FEV_1 of 1.5 L may have the same or better FEV_1 after lobectomy if the main bronchus of the affected lobe has been occluded completely at the time of testing before surgery. The oxygenation of blood of such a patient may be improved by the removal of a nonfunctioning lung or lobe through which considerable right-to-left shunt exists (figure 26-19).

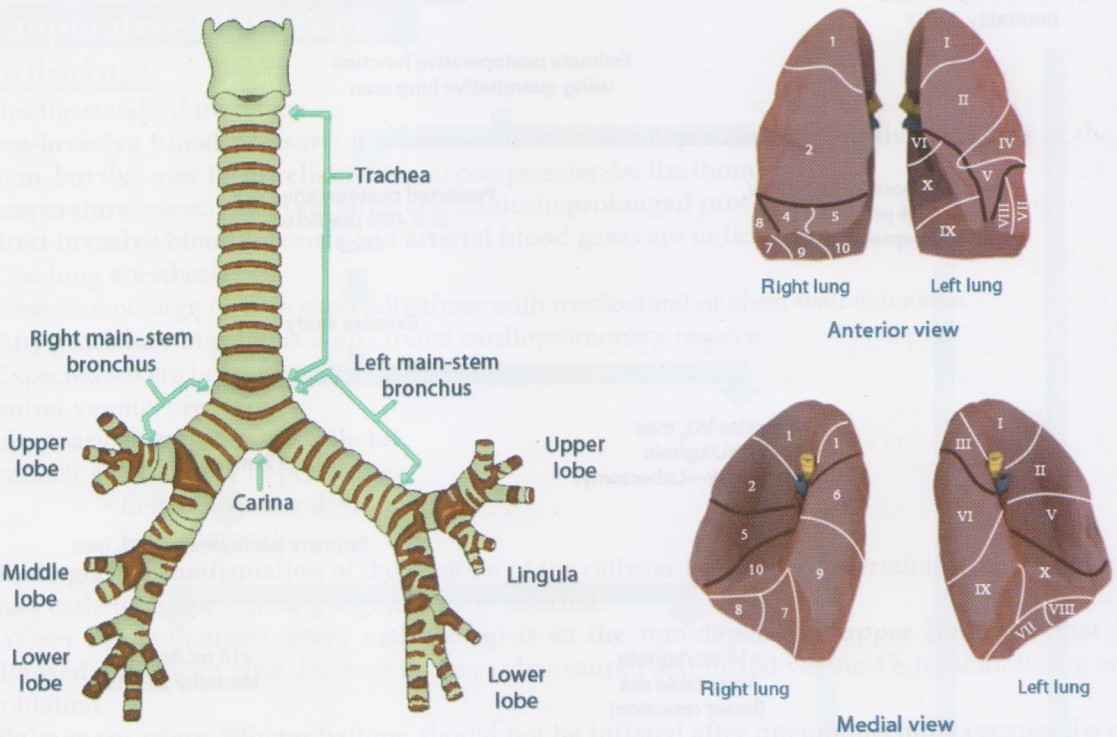


Figure 26-19: The tracheo-bronchial tree and broncho-pulmonary segments

b) Cardio-pulmonary Exercise Testing:

This test requires a patient to be able to pedal a bicycle ergometer and breathe through a mouthpiece. Increasing exercise to the peak allows calculation of maximum oxygen uptake expressed in mL/kg/min. Patients with VO_2 max >15 mL/kg/min have been able to withstand lobectomy whereas a predicted postoperative VO_2 max > 10 mL/kg/min is required to contemplate pneumonectomy. Cardio-pulmonary exercise testing is discussed in more details in chapter "Cardiovascular Diseases".

c) Cardiopulmonary Risk Index:

It is a combination of:

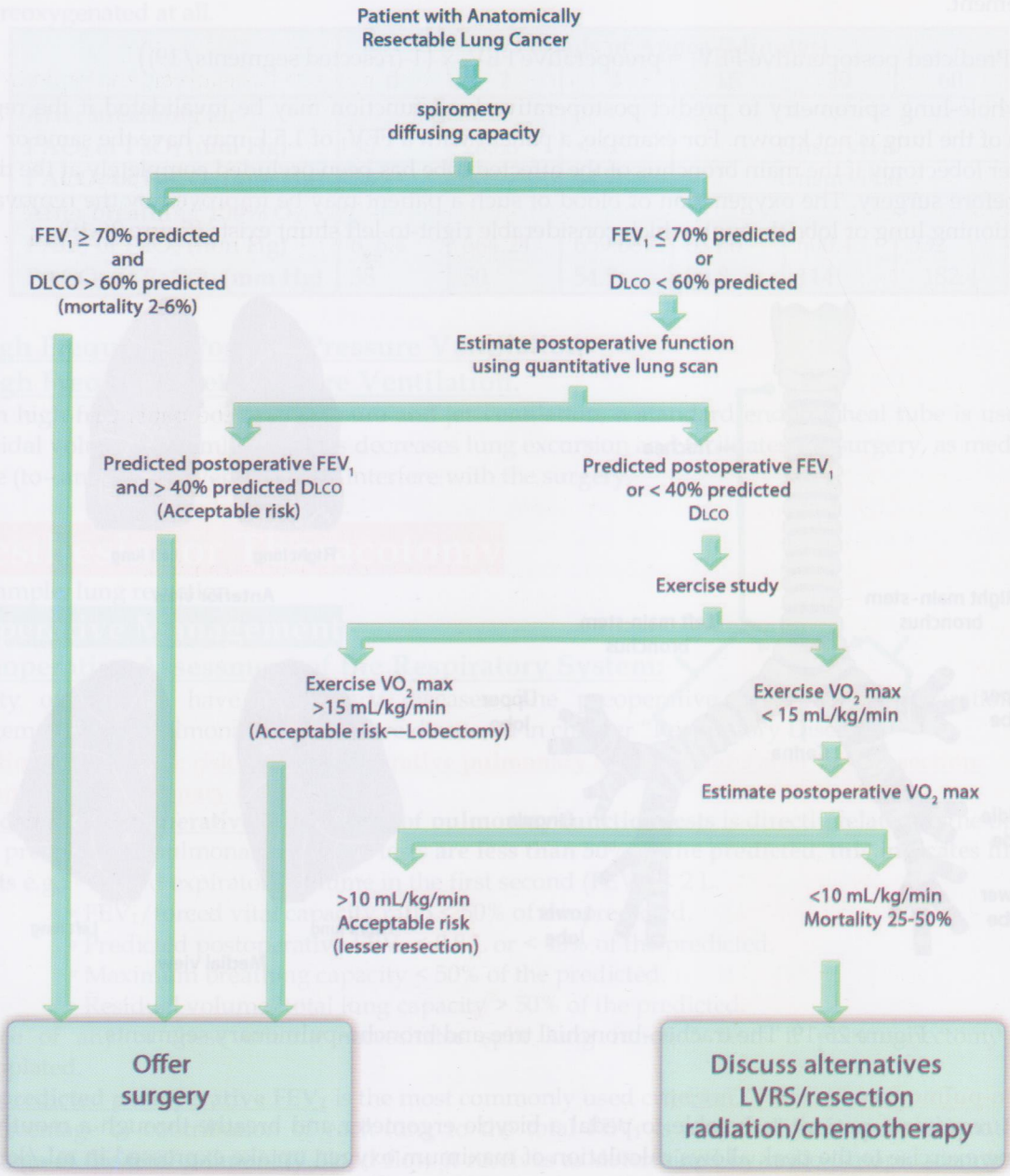
- The **Goldman cardiac index** value scored from 1 to 4. It is discussed in the chapter of "Cardiovascular diseases" and
- The **pulmonary risk index** scored from 1 to 6. It is discussed in the chapter of "Respiratory diseases".

Therefore, a combined total score of > 4 is highly predictive of postoperative complications after lung resection.

d) Predictive Respiratory Complication Quotient (PRQ)

It is calculated using a complex mathematical formula from the results of the patient's spirometry, carbon monoxide diffusion capacity, split lung function testing, and analysis of the effects of exercise on arterial blood gases. A PRQ < 2200 increases the risk of pulmonary complications.

The following algorithm (figure 26-20) can be used preoperatively to determine the need for preoperative investigations in a patient subjected to a surgery of lung resection.



LVRS: Lung volume reduction surgery
DLCO: Diffusion capacity of carbon monoxide

Figure 26-20: An algorithm showing the need for preoperative investigations before lung resection

2) Preoperative Patient Preparation:

Preoperative preparation of a patient with respiratory disease is discussed in more details in the chapter of "Respiratory Diseases".

Additional management includes:

1- Preoperative **patient nutrition and esophageal lavage** for cases of **esophageal surgery.**

2- Preoperative measures to **avoid deep venous thrombosis** e.g., low dose subcutaneous heparin.

3- Preoperative equipment for **airway management** should be available e.g., in addition to the basic equipment, variable sized single- and double lumen tubes, a flexible fiberoptic bronchoscope, a small diameter tube exchanger, continuous postoperative airway pressure (CPAP) delivery system and an anesthesia circuit adaptor for administering bronchodilators.

4- If epidural analgesia is planned postoperatively, it is better to put **the epidural catheter pre-operatively while the patient is awake** as this decreases neurological complications.

5- **Venous access:**

- At least one large bore i.v. cannula (14-16 gauge) is mandatory.
- Central venous access (preferably on the side of the thoracotomy), a blood warmer, and rapid infusion devices are needed if extensive blood loss is anticipated.

3) Premedication:

1. Sedatives: No or minimal doses are given if moderate to severe pulmonary disease is present.
2. Anticholinergics e.g., atropine 0.5 mg i.m. or glycopyrrolate 0.2 mg i.m. are controversial because they are given to decrease the copious secretions, but inspissated secretions and broncho-dilatation may occur (increasing the dead space).

Intraoperative Management

Monitoring:

Besides the standard monitors,

1- Non-invasive blood pressure: It is measured from **the dependent arm**, if the patient is in the lateral position, but this may be **unreliable** due to compression by the thorax.

2- Temperature: especially in **children** and adults in **prolonged** procedures.

3- Direct invasive blood pressure and arterial blood gases are indicated in:

- One lung anesthesia.
- Resection of large tumors especially those with mediastinal or chest wall extension.
- Any procedure in patients with limited cardiopulmonary reserve.
- Expected severe hemorrhage.

4- Central venous pressure.

5- Pulmonary artery pressure catheter.

Indications: ▫ Pulmonary hypertension
▫ Left ventricular dysfunction
▫ Corpulmonale.

- **Radiographic confirmation** of the position of the catheter is useful in ascertaining that the pulmonary artery catheter is not in a lung segment to be resected.
- When the pulmonary artery catheter tip is in **the non-dependent upper lung** and that lung is **collapsed,** it causes a false decrease in the cardiac output and mixed venous O_2 tension during one lung ventilation.
- **Pulmonary artery catheter balloon** should **not be inflated after pneumonectomy** because the remaining pulmonary vasculature has a significantly decreased cross-sectional area, as balloon inflation can acutely increase right ventricular afterload and decrease left ventricular preload.

Induction of Anesthesia:

Smooth induction is indicated with adequate **preoxygenation**. **Avoid the pressor response** and bronchospasm of intubation by deepening of anesthesia.

Intubation is performed by either: ▫ ordinary endotracheal tubes for most thoracotomies or
▫ one-lung ventilation in some cases.

Patient Position:

After induction in the supine position, the patient is turned to one of the following positions:

a) The Lateral Decubitus Position:

- It is indicated in most lung resections (posterior thoracotomies) and esophageal surgery.

• The patient is turned laterally with the diseased side uppermost.
• **The patient's head** must be kept in a neutral position to prevent excessive lateral rotation of the neck and stretch injuries to the brachial plexus. The head should be supported on a head support. **The dependent eye and ear** must be checked frequently for external compression to avoid corneal abrasion, retinal artery thrombosis, and pressure necrosis of the ear cartilage.
• **The lower arm** is flexed while **the upper arm** is supported on an armrest or foam cradle. For high thoracotomies, the nondependent arm may be elevated above the shoulder plane in front of the head pulling the scapula away from the operative field for more exposure. The arm should not be abducted greater than 90 degrees to avoid nerve injury due to excessive traction. The **pulse and blood pressure in the dependent arm** should be frequently monitored for early detection of compression of axillary neurovascular structures. If hypotension is detected in the dependent arm, it may be due to either hypotension of the patients or due to compression of the axillary neurovascular structures. This can be differentiated by comparison with the nondependent arm.
• Pillows are placed between **legs** (at knees) to prevent pressure damage with the dependent leg slightly flexed at the knee to minimize excessive pressure on bony prominences and stretch of the lower extremity nerves.
• A cushion (axillary roll or better name **chest roll**) is placed just caudad to the dependent axilla to avoid injury to the brachial plexus (figure 26-21). The chest roll should never be placed in the axilla. Its purpose is to ensure that the weight of the thorax is borne by the chest wall caudad to the axilla rather than by the axilla itself.
• When a **kidney rest** is used, it must be properly placed under the dependent iliac crest to prevent inadvertent compression of the inferior vena cava.
• Physiological effects of the lateral position are discussed above in details (see before).

b) Prone Position:

• It is preferred by some surgeons in some cases, as it allows drainage of secretions from the diseased lung towards the trachea without soiling the other lung.
• The shoulders and pelvis are supported to prevent pressure on the abdomen, which increases intra-abdominal pressure impairing lung base expansion. This decreases the venous return to the heart. The arm on the operative side hangs over the edge of the operating table, so that the scapula is pulled away from the site of surgery (figure 26-22).
• Physiological effects of prone position are discussed in more details in chapter "Respiratory Diseases".

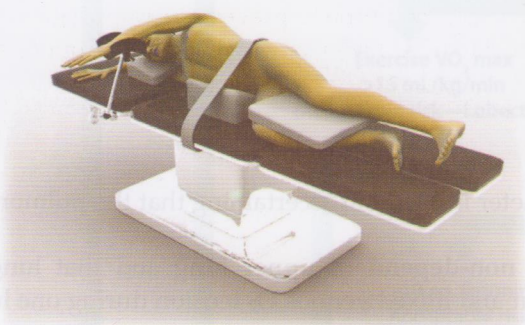


Figure 26-21: Lateral decubitus position



Figure 26-22: Prone position

Maintenance:

Balanced anesthesia is used consisting of:

N_2O:

It is usually **avoided** because: it causes an obligatory decrease in FiO_2,
it inhibits hypoxic pulmonary vasoconstriction (HPV) reflex, and
it increases the pulmonary hypertension in some patients.

If it is used, it should be only less than or equal to 40-60%.

Volatile agents:

Halothane, isoflurane, sevoflurane, or desflurane can be used.

Advantages: ▫ Potent dose-related broncho-dilatation.
▫ Depression of airway reflexes.

- The ability to use high FiO_2.
- The capability of relative rapid adjustments in the anesthetic depth.
- They have a minimal effect on HPV reflex in doses < 1 MAC.

Opioids:

Advantages:
- Generally, minimal hemodynamic effects.
- Depression of airway reflexes.
- Residual postoperative analgesia.

Muscle Relaxants and Controlled Mechanical Ventilation:

- They are important **in preventing effects of open pneumothorax** (paradoxical breathing and mediastinal shift) as discussed above.
- **During rib approximation, hand ventilation** is helpful in avoiding injury to the lung parenchyma from suture needles after lobectomy or wedge resection if a single lumen tube is being used.
- Before completion of chest closure, **all** the remaining **lung segments** should be **fully expanded manually under direct vision.**
- Controlled mechanical ventilation is then resumed and continued until chest tubes are connected to the suction.

Intraoperative Problems:

1) One-Lung Ventilation:

At first two-lung ventilation is maintained until the pleura is opened. Then one-lung ventilation is applied to the dependent lung.

The following measures should be considered to prevent or treat hypoxemia if it occurs during OLV:

1. **FiO_2 of 1.0** (i.e., 100% O_2) should be used. The PaO_2 during OLV should be between 150-250 mm Hg.
2. **Ventilatory Strategy (ventilatory setting) for OLV:**

- **Tidal volume:** With OLV, the **tidal volume** should be **8-12 mL/kg** (the same as two-lung ventilation), to preserve the tidal volume in the dependent lung.

Low tidal volume might produce **atelectasis** in the ventilated lung (reduced functional residual capacity) and increases in the degree of **shunt,** while **high tidal volume** might shift blood flow to the non-dependent lung (**similar to** application of positive end-expiratory pressure **"PEEP"**) to increase the **trans-pulmonary shunt.**

- **Respiratory rate:** should be adjusted to keep **$PaCO_2$ of 35 ± 3 mm Hg** because hypocapnia inhibits the HPV reflex in the non-dependent lung. Hypercapnia is acceptable (if it occurs), but not with hypoperfusion and acidemia.
- **Inspiratory: expiratory (I: E) ratio:** should permit enough expiration time to prevent air trapping.
- **Inspiratory flow rates:** should be reduced to allow less turbulence, lower positive peak inspiratory and inflation pressures.
- **Peak airway pressure:** should be **< 30-40 cm H_2O.**
- **Continuous positive airway pressure (CPAP) and positive end-expiratory pressure (PEEP):**
  - Some prefer giving **5-10 cm H_2O CPAP to the collapsed lung by differential lung ventilation**. This is **the most effective** when there is partial re-expansion of the lung, which unfortunately can interfere with the surgery.
  - Others prefer giving **5-10 cm H_2O PEEP to the ventilated lung,** but this can divert the blood to the non-ventilated lung (especially if large PEEP is used) resulting in hypoxia; therefore, it is preferred to use PEEP with **CPAP to the collapsed lung by differential lung ventilation.**
- **Recently, some debates** are aroused from the possibility of application of low tidal volume to the ventilated lung to apply **lung protective strategy in the operating room**, and prevent over-distention and stretching of the lung parenchyma and so, decrease the possibility of acute lung injury, but still the risk of atelectasis may occur due to the low tidal volume.

Some advocate the use of **low tidal volume (6-8 mL/kg) with PEEP (5 cm H_2O)** and **high respiratory rate** because this causes dynamic hyperinflation of the ventilated lung and keep normal $PaCO_2$.

3. **Keeping the period of OLV to a minimum.**
4. **Immediate re-expansion** of the collapsed lung should be done if hypoxemia persists.
5. **Search for a possible cause: e.g.,**
   - **Repeated fiberoptic bronchoscopy** through the tracheal lumen to **revise the position** of the endo-bronchial tube (or bronchial blockers) relative to the carina, which can be changed as a result of surgical manipulation or traction.

- **Both lumens** of the tube should also be **suctioned** to exclude excessive secretions, or obstruction. If blood is present in the airway, instillation of 3-5 mL of $NaHCO_3$ into the tube may facilitate the removal of clots.
- **Pneumothorax on the dependent ventilated side** should be considered. It usually occurs after extensive mediastinal dissection or with high peak inspiratory pressures.

6. Periodic inflation of the collapsed lung with O_2 i.e., **intermittent two-lung ventilation.** It is better to **ventilate manually** to determine whether higher or lower tidal volume/inspiratory pressures are beneficial.

7. **Early ligation or clamping of the ipsilateral pulmonary artery** during pneumonectomy is rarely needed.

8. Continuous **O_2 insufflation into the collapsed lung:** Three L/min allowed to circulate freely will often increase arterial O_2 saturation by 3-4%.

9. **Avoid fluid overload**.

10. **Avoid factors which inhibit HPV reflex** such as:

- Very high or very low **PAP**.
- **Hypocapnia.**
- High or very low **mixed venous PO_2.**
- **Vasodilators** e.g., nitroglycerin, nitroprusside, β agonist, dobutamine, or Ca^{++} channel blockers.
- **Inhalational anesthetics: Total intravenous anesthesia is preferred,** as it does not affect HPV reflex.

11. Recently, **nitric oxide is used.** It causes **vasodilation in the dependent lung** and so it increases the effect of the HPV reflex in the non-dependent lung. This decreases the degree of the shunt.

If **almitrine** bimesylate (a peripheral chemoreceptor agonist) is used i.v. in low doses (0.3 μg/kg), the **HPV reflex is increased in the non-dependent lung** decreasing the degree of the shunt. Avoid a high dose of almitrine 13 μg/kg because it decreases the HPV reflex.

Therefore, **a combination of inhaled nitric oxide and an i.v. low dose almitrine** eliminates the shunt and corrects the hypoxia.

2) Alternatives to One-Lung Ventilation:

such as apneic oxygenation, high frequency positive pressure ventilation, or high frequency jet ventilation (see above).

3) During Surgical Technique:

1. During rib spreading, maximal stimulation occurs. It needs **maximal anesthetic depth and muscle relaxation**.
2. Surgical manipulation may cause **vagally-mediated bradycardia** that may need i.v. atropine.
3. During lung resection, **the bronchial stump is tested for an air leak under water** by transiently sustaining 30-40 cm of positive airway pressure.
4. During closure, a chest tube connected to an under water seal may be placed after pneumonectomy (but not always) to ensure air or fluid drainage in the postoperative period.

4) Intraoperative Fluid Therapy:

- Opening of the chest causes **loss of the negative pleural (intra-thoracic) pressure, which decreases venous pressure**. This is avoided by **i.v. fluid bolus.**
- **Generally**, i.v. fluids should be **restricted** in patients undergoing pulmonary resections as excessive fluid administration in the lateral decubitus position produces **lower lung syndrome** i.e., **gravity-dependent transudation of fluid** into the dependent lung. This increases intrapulmonary shunting and hypoxemia especially with one-lung ventilation.

Postoperative Management and Intensive Care Considerations

1) General Care:

Patient care should be in the **intensive care unit**, usually overnight or for a longer time to detect postoperative complications. General care applied includes:

- Maintaining **semi-upright position** (> 30 degrees).
- **Physiotherapy** to aid lung expansion and cough.
- O_2 supplementation 40-50% (humidified).
- Close hemodynamic and ECG **monitoring.**
- Postoperative **chest x-ray**.

2) Extubation:

- Most patients are extubated early to decrease the risk of pulmonary barotrauma (especially blowout of the sutured line) and to decrease the risk of pulmonary infection.

• Patients with marginal pulmonary reserve should be left intubated until standard extubation criteria are fulfilled.

• **If a double-lumen tube** was used for one-lung ventilation, it may be **replaced with a regular single-lumen tube** at the end of surgery. A **catheter guide (tube exchanger)** should be used if the original laryngoscopy was difficult.

3) Postoperative Analgesia:

Postoperative analgesia is important as it minimizes postoperative pulmonary complications, allowing the patient to breathe deeply, cough effectively, and ambulate.

1. **Patient controlled analgesia:** Small i.v. doses of opioids are more preferred than large i.m. doses.
2. **Injection above and below the thoracotomy incision** by:
   - injection under direct vision intraoperatively or
   - local infiltration postoperatively.
3. **Intercostal block** by:
   - local anesthetics or
   - cryo-analgesia probe.

It may be used intraoperatively to freeze the intercostal nerves (cryo-neurolysis) causing long lasting anesthesia as maximal analgesia occurs after 24-48 hours and lasts for one month (as nerve regeneration occurs again).

4. **Epidural narcotics (lumbar or thoracic)** such as morphine or fentanyl. Doses and complications are discussed in the chapter of "Pharmacology of Anesthesia & Intensive Care".
5. **Intra-pleural (inter-pleural) analgesia**. It causes inconsistent results due to:
   - presence of a thoracotomy chest tube.
   - presence of blood within the pleura.

4) Postoperative Complications:

A) Respiratory Complications:

1- Postoperative Hypoxemia and Respiratory Acidosis: due to:

- **Atelectasis,**
- **Shallow breathing 'splinting'** because of the incisional pain,
- **Gravity-dependent transudation of fluid** into the dependent lung,
- **Re-expansion edema of the collapsed non-dependent lung** usually occurring with rapid re-inflation of the lung,
- **Preexisting lung disease,** and
- **Accumulation of fluid and air in the pleural cavity.**

2- Air Leak and Broncho-Pleural Fistula:

• **Air leaks** from the operative hemithorax are common after segmental and lobar resection because fissures are usually incomplete; therefore, after resection, small channels are left. Most air leaks stop after a few days.

• **Bronchopleural fistula**: There is a sudden large air leak from the chest tube and it may be associated with increasing pneumothorax and partial lung collapse. It occurs either:

- **within the first 24-72 hours**, due to **inadequate surgical closure** of the bronchial stump or
- **late**, due to **necrosis** of the suture line by **infection** or **inadequate blood flow**.

3- Torsion of a Lobe or Segment:

• It is rare. When torsion occurs, the remaining lung on the operative side expands occupying the hemithorax and occluding the pulmonary vein, with subsequent venous outflow obstruction leading to hemoptysis and infarction.

• Diagnosis is by:
- An enlarged homogenous density on the chest x- ray.
- Closed lobar orifice on bronchoscopy.

B) Postoperative Hemorrhage:

It occurs in 3% after thoracotomies resulting in mortality in 20% of cases.

Clinical picture:
- Increased chest tube drainage (> 200 mL/h).
- Hypotension and tachycardia.
- Decreased hematocrit.

Treatment: Immediate re-exploration is needed.

C) Cardiovascular Complications:

1- Postoperative supraventricular tachycardia.

2- Postoperative acute right ventricular failure because rapid fluid accumulation in the pleural cavity causes mediastinal shift and lung compression that leads to right ventricular failure.

3- Acute herniation of the heart into the operative hemithorax.

Cause: It occurs via the **pericardial defect** left after a radical pneumonectomy. On presence of a large pressure difference between the 2 hemi-thoraces, herniation into the operative side occurs.

Clinical picture:

a- Herniation into the right hemi-thorax causes:
- Sudden **severe hypotension.**
- **Increased central venous pressure** (due to torsion of the venous input).

b- Herniation into the left hemi-thorax causes:
- Sudden compression of the heart at the atrio-ventricular groove leading to **hypotension, ischemia, and infarction**.

A chest x-ray shows a shift of the cardiac shadow into the operative hemithorax.

D) Nervous System Complications:

1- Nerve injury: Extensive mediastinal dissection can injure:
- **the phrenic nerve (or even the diaphragm itself)** resulting in elevation of the ipsilateral hemi-diaphragm and difficulty in weaning from the ventilator.
- **the vagus nerve.**
- the **left recurrent laryngeal nerve** resulting in hoarseness.

2- Paraplegia: due to:
- Sacrificing (**cutting**) the left lower **intercostal arteries** producing **spinal cord ischemia.**
- **Epidural hematoma** if surgical dissection has accidentally involved the epidural space through the chest cavity.

Special Consideration for Thoracotomies

1) Lung Tumors

Clinical Picture:

- **Cough, hemoptysis**, dyspnea, wheezes and weight loss.
- Post-obstructive **pneumonia** resulting in fever and productive sputum.
- Pleuritic chest pain or **pleural effusion** due to pleural extension.
- Involvement of **mediastinal structures** with compression of:
  - **the recurrent laryngeal nerve** resulting in hoarseness.
  - **the sympathetic chain** resulting in Horner's syndrome.
  - **the phrenic nerve** elevating the hemi-diaphragm.
  - **the esophagus** resulting in dysphagia.
  - **the superior vena cava** resulting in superior vena cava syndrome.
  - the heart resulting in **epicardial effusion or cardiomegaly.**
  - the C_7-T_2 roots of the brachial plexus by apical tumor causing pain at the shoulders and arms (pancoast syndrome).
  - the trachea resulting in its displacement and may be difficult intubation.

- **Secondaries** in the brain, bone, liver, and adrenal gland.
- **Para-neoplastic syndrome:** may occur with small cell carcinoma (oat cell carcinoma) due to either ectopic hormone production or immunological cross-reactivity:
  - Ectopic hormone production such as:
    - **Cushing's syndrome** due to adreno-corticotropic hormone (ACTH) secretion.
    - **Hyponatremia** due to arginine vasopressin secretion.
    - **Hypercalcemia** and hypophosphatemia due to parathyroid hormone secretion.
    - **Carcinoid tumor**
  - Immunological cross-reactivity between the tumor and normal tissues leading to antibody production such as:
    - **Eaton-Lambert (myasthenic) syndrome**.
    - **Hypertrophic osteo-arthropathy**.
    - **Polymyositis**.
    - **Migratory thrombo-phlebitis**.
    - **Non-bacterial endocarditis**.

Treatment:

- **Chemotherapy.** It has side effects such as immunosuppression with possibilities of infections, anemia, leucopenia, thrombocytopenia, pulmonary fibrosis, renal and hepatic toxicity, and nervous toxicity.
- **Radiotherapy.** It may produce stiffness of the neck, difficult intubation, and lung fibrosis.

These complications should be kept in mind during preoperative assessment of patients with cancer.

- Surgical removal:
  - **Lobectomy**: It is removal of one lobe, which is performed for most lesions e.g., bronchial carcinoma and tuberculosis.
  - **Segmental or wedge resection:** for small peripheral lesions.
  - **Pneumonectomy:** for lesions in the left or right main bronchus or tumors extending to the hilum.
  - **Sleeve resection:** for proximal lesions with a poor pulmonary reserve (alternative to pneumonectomy) in which the involved lobar bronchus together with a part of the right or left main bronchus is resected and the distal bronchus is re-anastomosed to the proximal bronchus or the trachea.
  - **Sleeve pneumonectomy**: for tumors involving the trachea.

2) Lung Infections

such as bronchiectasis or lung abscess. They may be surgically resected.

Anesthetic Considerations:

1- Rapid sequence induction with a **double-lumen tube** while the patient is in the **semi-upright position** with the affected lung in a dependent position **to prevent soiling of the healthy lung.**

2- Repeated suction is needed for the diseased lung.

3) Massive Pulmonary Hemorrhage

It is usually treated by tamponading the site of bleeding.

Definition:

Massive pulmonary hemorrhage is considered if > 500-600 mL of blood loss occurs from the tracheo-bronchial tree within 24 hours.

Anesthetic Considerations:

1- Emergency measures should be taken such as:

- **ABCD protocol**.
- **Multiple large i.v.** cannulas.
- **Maintaining the lateral decubitus position** as much as possible with the affected lung in a dependent position **to tamponade the bleeding.**
- **A bronchial blocker or a Fogarty catheter** is placed.

2- Search for possible causes as tuberculosis, bronchiectasis, or tumors after trans-bronchial biopsies. **Rigid or fiberoptic bronchoscopy** may be applied to allow for:

- Embolization of the involved bronchial arteries.
- Trans-bronchial biopsies.
- Laser coagulation.

3- Avoid premedication. If the patient is already intubated or a bronchial blocker is placed during resuscitation, sedation is needed to prevent coughing and straining.

4- Induction and intubation:

- **Preoxygenation** with 100% O_2.
- **Awake intubation** is preferred because patients usually **swallow** a large amount of **blood** and should be considered to have **a full stomach**.
- **Rapid sequence induction** is performed in the semi-upright position with cricoid pressure using **ketamine and succinylcholine.**

5- One-lung ventilation (OLV) can be applied by:

- A large double-lumen endobronchial tube.
- A univent, if introduction of a double lumen tube has been difficult or during emergency resuscitation.

OLV is important to: • protect the normal lung from blood and
• allow suction of each lung separately.

4) Pulmonary Cysts and Bullae

They may be treated by surgical resection.

Anesthetic Considerations:

- Recurrent pneumothorax.
- They may rupture during anesthesia (especially if N_2O is used as it expands air spaces) causing **tension pneumothorax.**

5) Broncho-Pleural Fistula

It is a connection between the tracheo-bronchial tree and the pleural cavity.

Anesthetic Considerations:

- Assessment of **causes** is important such as:
  - **post-pneumonectomy** due to breakdown of a bronchial stump or anastomosis,
  - **rupture of a pulmonary abscess** into a pleural cavity,
  - pulmonary **barotrauma**,
  - **trauma,**
  - **tumor,** or
  - **spontaneous** rupture of a bulla.
- There is usually **empyema** (pus collection in the pleural cavity), which should be drained as much as possible preoperatively. Patients are usually cachectic and dehydrated with poor pulmonary function. Due to empyema, there is a risk of lung contamination on the other side; therefore, **OLV** is necessary.
- There is a risk of **tension pneumothorax.**
- **Before closure of the fistula, spontaneous ventilation** during induction and maintenance is recommended because controlled ventilation will push the gas during inspiration to the site of the fistula with resultant decrease in the ventilation of the normal parts of the lung and hypoxemia. **There is inability to effectively ventilate the patient with positive pressure due to a large air leak via the fistula.** If the chest tube drain is partially patent, it increases the intra-pleural pressure resulting in a risk of squeezing the tracheo-bronchial tree, so the other lung may be contaminated.
- Some recommend **awake intubation with a double lumen tube** (due to the presence of a large air leak) but **rapid sequence induction** is commonly used.

N.B.: Other causes of empyema include:
- Lung infection.
- After esophageal perforation or thoracotomy.

6) Pleurectomy and Pleurodesis

Definitions:

- **Pleurectomy:** is surgical removal of the pleura via an antero-lateral thoracotomy.
- **Pleurodesis:** is an induced adhesion of the pleura achieved by introduction of iodized talc via a thoracoscope or by making abrasions of the pleura with a gauze swab via a small thoracotomy incision.

Anesthetic Considerations:

- Search for **causes** as recurrent pneumothorax which is the most common cause.
- The patient may have an **underlying pulmonary disease**.
- The patient usually has **severe hemorrhage**.
- **Avoid N_2O and controlled mechanical ventilation** if there is an air leak or cyst.

7) Removal of an Inhaled Foreign Body

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It is discussed in the chapter of "Otorhinolaryngology".

Anesthesia for Tracheal Resection

Anesthetic Considerations:

a- Preoperative:
- The cause.
- Tracheal (airway) obstruction.

b- Intraoperative:
- Intubation.
- Ventilation during resection.

c- Postoperative:
- Patient position (flexed neck).

Anesthetic Management:

Preoperative Management:

1- **Preoperative assessment of the cause** by history, examination, and investigations such as:

- **Tracheal stenosis** due to a penetrating or blunt trauma, prolonged endotracheal intubation, or tracheostomy.
- **Tumors** especially squamous cell carcinoma or adenoid cystic carcinoma.
- **Congenital** anomalies.

2- Preoperative assessment of the **degree of the tracheal obstruction:**

- **Progressive** airway obstruction causes dyspnea, wheezes, and stridor which increases on lying down and with exertion.
- **CT scan and chest x- ray** (figure 26-23).
- **Flow-volume loops**. They are discussed in the chapter of "Respiratory Diseases".

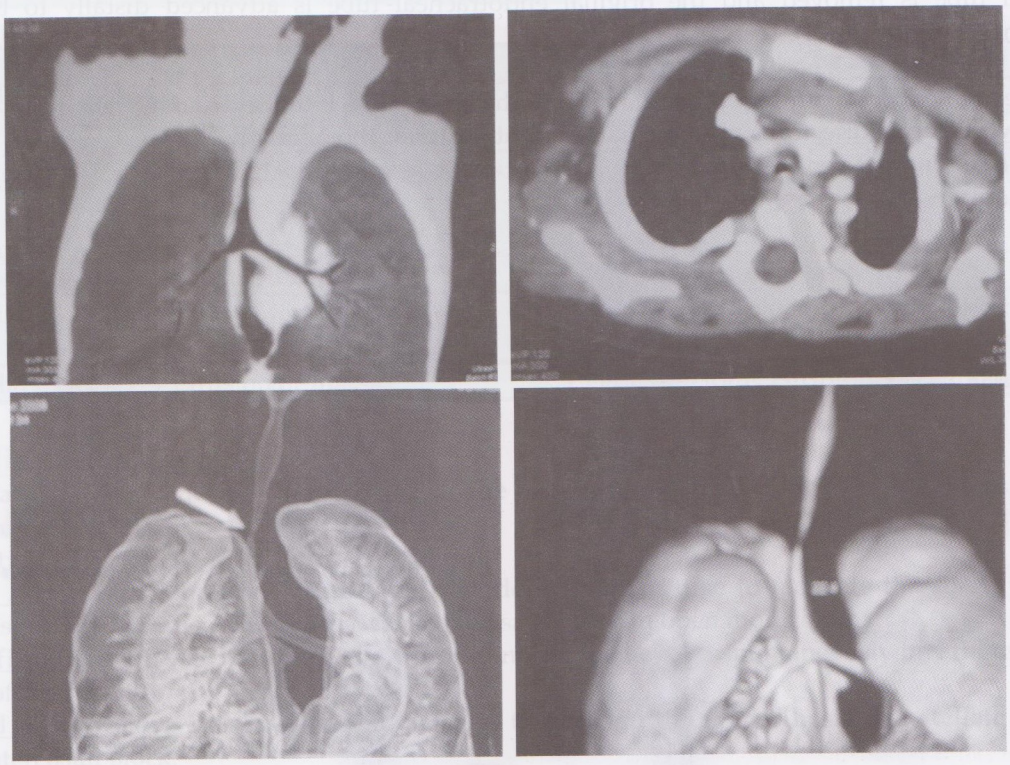


Figure 26-23: CT scan images showing tracheal stenosis; coronal (upper left), transverse (upper right) and 3-D reconstruction image (lower images)

3- Premedications:

- Sedatives: **No or minimal sedation** is needed as patients have a moderate to severe airway obstruction.
- Anticholinergics: They are controversial as they can dry secretions, but they make them inspissated.

Intraoperative Management:

Monitoring:

Besides the standard monitors,

- Invasive arterial blood pressure (with arterial blood gas analysis). The **left radial artery is preferred** in lower tracheal resections because there is a possibility of compression of the innominate artery leading to compression of the right radial artery.

Induction:

Slow inhalational induction (due to airway obstruction) should be applied with 100% O_2 and halothane or sevoflurane.

Lidocaine 1-2 mg/kg i.v. may be given to deepen the anesthesia. After the patient reaches deep anesthesia:

- The surgeon may do **rigid bronchoscopy** to evaluate and possibly dilate the lesion.
- **Laryngoscopy is performed and intubation** is done with a suitable **small endotracheal tube** that can be passed distal to the obstruction whenever possible.

Maintenance:

It is performed as usual for general anesthesia.

Intraoperative Problems:

Ventilation during tracheal resection is performed as follows:

a- **For High Tracheal Resections** via a collar incision:

1- A Sterile Armored Tube:

The surgeon divides the trachea in the neck below the lesion then advances a sterile armored tube into the distal trachea for ventilation during resection.

After completion of the resection, the posterior part of the trachea is re-anastomosed first then the armored tube is removed and the original endotracheal tube is advanced distally to bypass the anastomosis (figure 26-24).

2- High Frequency Jet Ventilation:

It can be applied by passing a jet cannula beyond the obstruction into the distal trachea.

b- **For Low Tracheal Resections** via a median or right posterior thoracotomy.

1- High frequency jet ventilation.

2- Cardiopulmonary bypass.

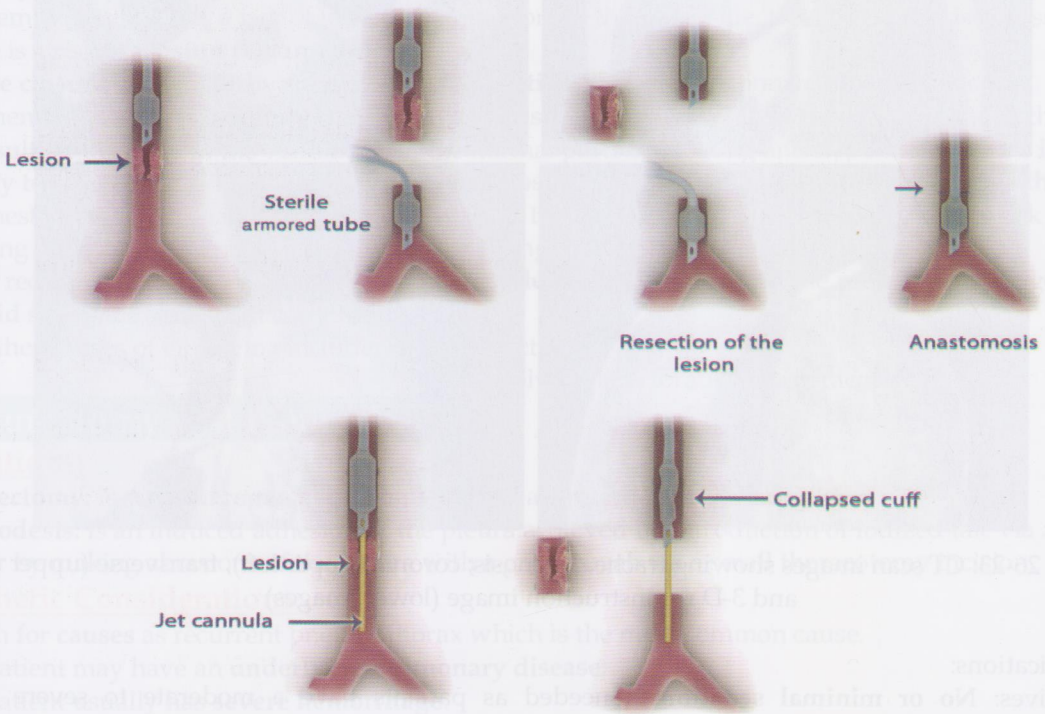


Figure 26-24: Ventilation during the tracheal resection by using another sterile tube (upper) or jet ventilation (lower)

Extubation:

Early extubation is desirable.

Postoperative Management:

The patient should be positioned with **the neck flexed**, immediately postoperatively, to decrease the tension on the suture line (figure 26-25).

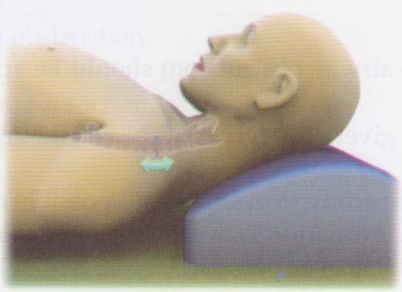


Figure 26-25: Postoperative patient position after tracheal resection

Anesthesia for Thoracic Telescopic Procedures

They include:

1- Thoracoscopy (Video-Assisted Thoracoscopy) (VAT).
2- Bronchoscopy (Fiberoptic and Rigid).
3- Mediastinoscopy.
4- Esophagoscopy (Fiberoptic and Rigid).

1) Thoracoscopy, Minimally Invasive Thoracic Surgery, or Video-Assisted Thoracoscopy (VAT)

Indications:

	a- Diagnostic	b- Therapeutic
1. Pleural diseases	Effusion , tuberculosis, or mesothelioma	Pleurectomy and pleurodesis.
2. Lung diseases	Interstitial pulmonary fibrosis, staging of tumors	Biopsy, laser ablation of bullae, segmental or lobar resection, cyst removal, abscess drainage, or closure of air leaks
3. Esophageal diseases	Staging for tumors	Vagotomy or myomectomy
4. Mediastinal diseases	Mass biopsy	Thymectomy or cervical sympathectomy for palmar hyperhydrosis
5. Pericardial diseases	Effusion or mass.	Pericardictomy (stripping or window)

Anesthetic Considerations:

1- **Preoperative** assessment and management of **the lesion** e.g., pleural effusion, lung disease, airway obstruction...etc.

2- Anesthetic Technique:

• **General Anesthesia: One-lung ventilation** by a double lumen tube to facilitate the surgery may be indicated especially for **apical lung diseases**. It is the same as with open thoracotomy.

• **Local Infiltration:** It is used in some centers for minor procedures in spontaneously breathing patients; with propofol infusion.

• **Regional Anesthesia:** It can be performed such as **thoracic epidural anesthesia and stellate ganglion block** or intercostal block.

3- Surgical Technique:

• Most procedures are done through 3 or more small incisions in the chest with the patient **in the lateral decubitus** position, where the thoracoscope is introduced into the pleural cavity.

• **If large structures** are resected, **a small subcostal incision** is made towards the end of the procedure to remove the resected tissues.

• Surgeons should be **ready for immediate open thoracotomy** if necessary.

• **Partial collapse of the lung** on the operated side occurs by allowing **air to enter through one of the thoracoscopic ports into the pleural cavity**.

Therefore, unlike laparoscopy, **there is no need for gas (CO_2) insufflation to collapse the lung** on the operated side because it is very dangerous. If the lung continues to be ventilated, very high intra-thoracic pressure during inspiration occurs leading to mediastinal distortion and cardiovascular collapse.

In very rare cases, CO_2 gas insufflation (i.e., **capnothorax**) is needed when the lung on the operated side is not collapsed using a double lumen tube with the following precautions:

- **The intra-thoracic pressure should be < 6 mm Hg (usually maintained at 2 mm Hg).**
- **The flow of CO_2 insufflation should be < 2 L/ min.**

Both allow hemodynamic stability.

- **Mechanical ventilation is mandatory.**

4- Complications of OLV during Thoracoscopy:

1- The usual **complications with OLV** may occur such as:

• Mal-position of the DLT.
• Incomplete deflation of the ipsilateral lung.
• Hypoxia.

2- **Pneumothorax,** which may be spontaneous or due to:

- Intra-pleural CO_2 insufflation causing a clinical picture similar to pneumothorax.
- Barotrauma.
- Surgical air leak.

3- **Pulmonary edema:** 3 types can occur:

a- **Negative pressure pulmonary edema**:

Due to • excessive intra-pleural suction on the non-ventilated side or
• excessive bronchial suction on the non-ventilated side.

Both produce more negative intra-pleural and intra-thoracic pressures with a subsequent increase in the venous return of the right ventricle and a decrease in the cardiac output of the left ventricle. This causes pooling of blood in the pulmonary capillaries, increasing pulmonary pressure and capillary leak.

b- **Re-expansion Pulmonary Edema:**

Due to • development of negative pressure pulmonary edema on rapid re-expansion of a collapsed lung by thoracoscopy,
• generation of O_2 free radicals during reperfusion, and
• decreased surfactant concentration leading to capillary leak.

c- **Paradoxical Pulmonary Edema:** (in the dependent ventilated lung)

Due to • excessive fluid administration resulting in fluid overload.

This is exaggerated during OLV due to:

- hypoxic pulmonary vasoconstriction reflex in the collapsed non-dependent lung directing the blood to the ventilated dependent lung,
- gravity effect, and
- over-inflation of the dependent lung resulting in capillary endothelial damage, which leads to capillary leak.

2) Bronchoscopy

Indications:

a- Diagnostic: • Diagnosis of an endobronchial mass.
• Staging of bronchogenic carcinoma.
• Obtaining a biopsy.

b- Therapeutic: • Removal of a foreign body (by a rigid type).
• Insertion of an endobronchial stent (by a rigid type).
• Resection of an endobronchial mass e.g., laser.
• Facilitation of endobronchial intubation in difficult cases (by a flexible type).
• Relieving airway obstruction due to tracheal stenosis or tracheomalacia (by a rigid type).

Types of Bronchoscopes and Anesthetic Management:

A- Fiberoptic (Flexible) Bronchoscopy:

It is discussed in the chapter of "Airway Management".

B- Rigid Bronchoscopy:

It is discussed in the chapter of "Otorhinolaryngology".

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3) Mediastinoscopy

Indications:

- For obtaining a tissue biopsy especially from a lymph node.
- For staging of lung malignancy.

Anesthetic Considerations:

1- Preoperative assessment of **the lesion** e.g., in lung malignancy, anemia, cachexia, and secondaries are common findings.

2- Preoperative detection of **contraindications** that prevent mediastinoscopy:

- Previous mediastinoscopy.
- A superior vena cava syndrome.
- Tracheal deviation.
- Aortic arch anomalies.
- Cerebro-vascular diseases.

3- **Surgical approaches:**

- **Trans-cervical approach** for the **superior mediastinum** is performed via a small incision at the supra-sternal notch for introduction of the scope inside the mediastinum behind the manubrium sterni. As the pleural space is generally not opened intentionally, a chest tube is not indicated, but occult pneumothorax may occur, which may require a chest tube.
- **Trans-thoracic approach** for **the lower left mediastinum** is performed via an anterior approach through the 2nd left intercostal space.

4- **Anesthetic techniques**:

- **General anesthesia** with an endotracheal tube and controlled mechanical ventilation is used now.
- **Local anesthesia and sedation** were used in the past.

5- **Blood pressure monitoring:** is important. The **left arm** is usually used **for blood pressure** monitoring because the innominate artery (on the right side) may be compressed during the procedure. Some physicians also apply **the pulse oximeter on the right hand to detect the compression** of the innominate artery where damping of the pulse oximeter trace occurs while the blood pressure trace on the left side remains accurate.

6- **Complications of mediastinoscopy:**

Cervical (superior) mediastinoscopy is more difficult and is associated with greater complications such as:

1. **Compression of the trachea and great vessels**, especially on the right side (aorta, innominate artery, right common carotid artery, or right subclavian artery) resulting in **vagally mediated reflex bradycardia**.
2. **Excessive hemorrhage** from the biopsy site or due to injury of a vascular structure (superior vena cava, azygos vein, innominate artery, pulmonary artery, or aorta); therefore,
   - **2 large bore i.v. cannulas** are inserted, one cannula **in the arm** and the other **in the leg**, because it is difficult to replace blood loss through cannulation in the upper body, as any fluid will escape into the mediastinum.
   - **2 units of blood** should be prepared.
   - **Local anesthesia should be avoided.**
   - If hemorrhage occurs, the mediastinum is **packed with swabs soaked in a weak epinephrine solution**. If vital signs are constant, the swabs are removed after 10 minutes and the mediastinoscope is reintroduced.

   If bleeding stops, a drain is left in place for at least 24 hours.

   If bleeding continues or hemodynamic instability occurs, immediate emergency thoracotomy via a postero-lateral approach is needed.
3. **Cerebral ischemia** from compression of the innominate artery (detected by plethysmography or pulse oximetry on the right hand).
4. **Pneumothorax**, which usually occurs postoperatively.
5. **Air embolism** (due to 30 degree head elevation). The risk is greatest during spontaneous ventilation and with N_2O.
6. Injury to adjacent structures such as **the recurrent laryngeal nerve, phrenic nerve, pleura, trachea, or esophagus.**

4) Esophagoscopy

Indications:

a- Diagnostic: • Cancer esophagus.
• Localization of the site of an esophageal pouch.

b- Therapeutic: • Removal of a foreign body (by the rigid type).
• Injection of sclerotherapy.

Types:

a- Fiberoptic (Flexible) Esophagoscopy:

It is used mainly for diagnostic procedures and injection of sclerotherapy.

b- Rigid Esophagoscopy:

It is used mainly for removal of a foreign body.

Anesthetic Considerations:

1- Preoperative assessment for the lesion especially **malignancy** as patients are **elderly** with coexisting diseases, cachectic, and dehydrated.

2- Premedications:

- No oral premedication is given.
- There is a risk of aspiration; so, antacids and H_2 blockers are given.

3- Anesthetic techniques:

- **Local analgesia and sedation** are usually used for **fiberoptic** esophagoscopy.
- **General anesthesia** is usually used for **rigid** esophagoscopy. **Rapid sequence induction** with cricoid pressure and cuffed endotracheal tube (a reinforced armored tube is preferred). The cuff of the endotracheal tube may **temporarily be deflated** to allow the esophagoscope to pass through the cricopharyngeal sphincter. **Good muscle relaxation** is needed to avoid intraoperative cough, which may cause esophageal perforation, teeth or cervical spine injury.

Awake extubation in the lateral position with the head down is performed.

4- Postoperative Care:

- Patients kept in the **semi-setting position**.
- **A chest x-ray** immediately after esophagoscopy to detect **esophageal perforation** (before oral fluid intake).
- **Humidified O_2.**
- No oral intake for 12-24 hours postoperatively.

Broncho-Alveolar Lavage

Indications:

Pulmonary alveolar proteinosis, which is due to increased surfactant production with failure to clear it. Dyspnea and bilateral consolidation in chest x-ray, are common.

Technique:

- Only **one lung is lavaged at a time, the worst lung first**, to allow the patient to recover for a few days before the other lung is lavaged.
- It is done **under general anesthesia** with a **double-lumen endobronchial tube**. The cuffs of the tube should be properly positioned and should make **a water-tight seal** to prevent spillage of fluid into the other side.
- The procedure is done in **the supine position,** although lavage with the lung in a dependent position helps to decrease soiling of the other lung, but this position can cause severe ventilation/perfusion mismatching.
- **Warm normal saline** is infused into the lung to be lavaged and is drained by gravity. Lavage is continued until the fluid returning is clear (about 10-20 L).
- At the end of the procedure, **both lungs are suctioned well**.

Lung Transplantation

The first successful (i.e., a patient left the hospital) single lung transplantation was performed in 1983 for idiopathic pulmonary fibrosis.

Types of Lung Transplantations

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There are 5 types of lung transplantation:

1- Single-lung transplantation.

2- Bilateral sequential lung transplantation. It involves the sequential performance of two single-lung transplants at one time.

3- Bilateral *en-bloc* lung transplantation.

4- Heart-lung transplantation.

5- Transplantation of lobes from living donors.

Indications

End-stage pulmonary parenchymal disease or pulmonary hypertension (i.e., a patient is unlikely to survive > 18 months).

1- Restrictive: Single lung transplantation is the procedure of choice.

Such as: • Idiopathic pulmonary fibrosis.

Because the remaining native lung is stiff and vasoconstricted, it will be relatively weakly ventilated and perfused; therefore, it is usually left without compromising the transplanted lung.

2- Obstructive: **Single lung transplantation** is chosen.
Such as: • chronic obstructive pulmonary disease (COPD).
• Alpha 1 antitrypsin deficiency.
• Pulmonary lymph-angiomatosis.
Hyperinflation of the remaining native lung causes a mediastinal shift and profound ventilation/perfusion mismatching. This makes single lung transplantation unsuitable, but clinical experience has showed that many emphysemic patients can be successfully treated with single lung transplantation (with considering this physiological disorder).
3- Infectious: **Double lung transplantation** is chosen.
Such as: • Cystic fibrosis (the most common indication in patients < 18 year old).
• Bronchiectasis.
Due to potential infectious cross-contamination of the transplanted lung, chronic infectious diseases represent the only absolute contraindication to single lung transplantation. However, single lung transplantation with contralateral pneumonectomy is performed and has been suggested as an alternative solution.
4- Vascular: **Double or single lung transplantation** is chosen.
Such as: • Primary pulmonary hypertension.
• Eisenmenger's syndrome due to: ▫ a chronic increase in pulmonary blood flow, or
▫ pulmonary venous hypertension.
Since the remaining native lung can usually be left intact without compromising the transplanted lung (which will receive the majority of the blood flow); so, single lung transplantation can be done in some patients.
5- Re-transplantation.

Q: What are the indications of single and double lung transplantation?
A: Whenever possible, single lung transplantation is performed due to the severe shortage of donor organs. The indications can be detected as above.

Criteria for Recipient Selection

1- Patients should have one of the previous indications as above.
2- **Patients should not have any contraindication** such as:
• Severe diseases of other systems.
• Mentally and psychologically unstable patients as they cannot follow strict regimens of rehabilitation and immuno-suppressive therapy.
N.B.: In the past, there are other contraindications, but they are no longer present as:
• Concomitant steroid therapy.
• Previous intrathoracic therapy.
• Mechanical ventilation.
• Right ventricular failure.

Criteria for Donor Selection

The donors are **usually brain-dead persons** most commonly after head-trauma.
1- **Lung criteria**: It should be **completely normal.**
It should be of the **same size.**
2- Blood **ABO** compatibility is essential.
3- **Hepatitis, human immuno-deficiency virus (HIV), and cytomegalovirus free.**

Results

Survival rates of lung transplantations:

	1 year	2 year	3 year	4 year
All transplants	71%	63%	57%	51%
Single	71%	62%	56%	49%
Double sequential	**73%**	66%	59%	55%
Double en-bloc	62%	55%	49%	45%

Anesthetic Management

It involves nearly the same principles of pneumonectomy.

Preoperative Management

1) Preoperative Assessment of Lung Lesions:

It is discussed in details in the chapter of "Respiratory Diseases".

Patients typically have: dyspnea at rest or with minimal activity,
hypoxemia (PaO_2 < 50 mm Hg) i.e., respiratory failure,
progressive CO_2 retention i.e., respiratory failure, and
they may be ventilator-dependent.

2) Preoperative Assessment of Cardiovascular System:

It is discussed in details in the chapter of "Cardiovascular Diseases".

Patients should have **normal left ventricular function** and should be **free from coronary artery disease** by echocardiography and cardiac catheterization…etc.

Cor pulmonale does not necessarily require combined heart-lung transplantation, because right ventricular function may recover when pulmonary artery pressure normalizes. Patients with **Eisenmenger's syndrome require combined heart-lung transplantation.**

3) Preoperative Assessment of Other Systems to exclude contraindications.

4) Premedications and Drug Therapy:

Patients presenting for lung transplantation range from those who are compensated and awaiting at home for a suitable lung (on medical therapy as before e.g., bronchodilators, pulmonary vasodilators …etc) to those who are decompensated with mechanical ventilation support.

1- Sedatives:

They are usually **avoided**; if given, it should be in the operating room under direct observation of the anesthesiologist, either i.v. or i.m. (not oral as there is no enough time).

2- Aspiration prophylaxis.

3- Infection prophylaxis.

4- Immuno-suppression protocol.

It is similar to that of heart transplantation.

5) Patient Preparation:

a- Venous Access:

- **Two large bore i.v. catheters** (one in the wrist or forearm since the arms may be flexed during the procedure). Large bore cannulas are especially indicated in patients with:
  - a chronic infectious lung disease or
  - a history of previous intra-thoracic procedures

due to the potential brisk bleeding during dissection of pulmonary adhesions.

- Meticulous care must be taken on **removal of air bubbles** from i.v. infusion lines especially in patients with known or suspected **right to left shunts (to avoid paradoxical embolism)** due to presence of high right atrial pressure.

b- Proper Placement of Lumbar or Thoracic Epidural Catheters.

Epidural analgesia can be used intra- and postoperatively except:

- In patients anticoagulated preoperatively or
- In whom cardio-pulmonary bypass (CPB) is planned (the preoperative placement of an epidural catheter carries no adverse effects if emergent cardio-pulmonary bypass and heparinization are to be used).

Delaying placement of the epidural catheter until the postoperative period may actually increase the risk of complications because both hemodilution and immuno-suppression tend to promote coagulopathy.

c- Preoperative Preparation of the Equipment includes:

- An **anesthesia ventilator** capable of delivering a wide range of inspiratory: expiratory (I: E) ratios and respiratory rates.
- A **jet ventilator**, which is beneficial if the distal airway becomes disrupted.
- A **continuous positive airway pressure (CPAP) apparatus.**
- A **CPB machine**.
- A **sterile circuit** for the anesthesia machine and sterile tubing for the jet ventilation.

6) Patient Monitoring:

Monitors are nearly the same as those of cardiac surgery, in addition to the following considerations:

- **Strict aseptic** technique is used.
- **Invasive arterial blood catheter**: **A femoral artery** may be used instead of a radial artery under local anesthesia in the operating room because the radial artery pressure may become damped during the procedure due to positioning of the arms.
- **Central venous pressure catheter:** is usually inserted after induction because patients are usually unable to lie flat while awake.
- **Pulmonary artery catheter:** Its use is **routine** especially those that can measure **right ventricular ejection fraction and mixed venous O_2 saturation** due to the profound changes in pulmonary and systemic hemodynamics that often occur both during and after lung transplantation. In patients undergoing single lung transplant, pulmonary artery catheters **often migrate to the operative side** after the patient has been placed **in the lateral position,** even when **radiologically confirmed** to be positioned in the non-operative lung. Therefore, the surgeon should be reminded to palpate the pulmonary artery and **withdraw the catheter into its sterile protective sheath** just before cross-clamping the vessels (if it floats to the operative side) then it may be re-floated back into the pulmonary artery after transplantation.

  Due to tricuspid regurgitation (usually associated with pulmonary hypertension), there is a difficulty encountered in floating the pulmonary artery catheter and measuring the cardiac output and ejection fraction, as it may be distorted by the tricuspid valve.
- **Two-dimensional trans-esophageal echocardiography:** It is usually used to:
  - assess right ventricular ejection fraction and differentiate between right ventricular and left ventricular dysfunction.
  - assess blood flow in the pulmonary vessels before and after transplantation.
  - assess the fluid balance.

  Visualization of the right ventricle by trans-esophageal echocardiography in laterally positioned emphysematous patients is often poor.
- **Continuous measurement of pulmonary mechanics** by side-stream spirometry. It is valuable in early detection of reperfusion injuries and graft dysfunction.

Intraoperative Management

As with heart transplantation, proper timing and coordination are needed between the donor organ retrieval team and the transplant center because:

- Premature induction unnecessarily prolongs CPB (if needed).
- Delaying induction jeopardizes the graft function, by prolonging the donor's heart ischemia time, which is limited to 4-6 hours.

Complete aseptic techniques are used e.g., airway equipment such as:

- **Sterile anesthetic delivery tubing and handling with sterile gloves.**
- **Bacterial filters** are often used on the inhaled and exhaled limbs of the anesthetic delivery tubing.

Generally, there are **no specific recommendations regarding drugs** for induction and maintenance of anesthesia and skeletal muscle paralysis for lung transplantation. Drug-induced histamine release is undesirable, whereas drug-induced bronchodilatation is useful.

Induction:

- **Modified rapid-sequence induction** is chosen. **Prolonged preoxygenation** with 100% O_2 for 15-20 min is recommended. A non-depolarizing muscle relaxant such as **vecuronium, rocuronium, or even** a depolarizing muscle relaxant such as **succinylcholine** can be used.
- Induction agent as:
  - **Thiopentone**: It is avoided in patients with bronchospasm.
  - **Ketamine**: It is avoided in patients with pulmonary hypertension (but used in bronchospasm).
  - Etomidate: It is a cardiac stable agent.

  Then fentanyl 10-15 µg/kg or sufentanil 1-2 µg/kg is administered.
- Cricoid pressure may be applied.
- Hypotension is common after induction. It is treated by vasopressors (dobutamine) instead of a large fluid bolus.
- **A trans-esophageal probe** is placed after induction.

Intubation:

- For both single and double lung transplantation, use either:
  - a **left** endobronchial **double** lumen tube or
  - a single-lumen endotracheal tube with a bronchial blocker.
- For cystic fibrosis, first, **a large single lumen tube** is placed and through that, extensive bronchoscopically directed bronchial lavage and suction, due to presence of thick tenacious secretions, are performed. Then **a double-lumen tube** is placed. Good suction can not be done using a double lumen tube, as only small sized catheters can be placed inside it.

Maintenance:

100% O_2 + opioid infusion ± low-dose isoflurane + controlled mechanical ventilation and a muscle relaxant.

- **100% O_2** is used because:
  - The recipient's lung has little pulmonary reserve.
  - High PaO_2 causes **pulmonary vasodilation, which decreases the right ventricular afterload.**

  Acute oxygen toxicity to the transplanted lung has been reported in some cases; therefore, 100% O_2 is still **controversial.**
- **Opioid infusion** especially short acting agents such as fentanyl or sufentanil is recommended.
- **A low dose volatile agent** is usually avoided due to its theoretical effect on the inhibition of hypoxic pulmonary vasoconstriction, but the clinical use of small doses of isoflurane, sevoflurane, or desflurane is useful due to its bronchodilating properties without inhibition of the hypoxic pulmonary vasoconstriction reflex.
- **Controlled mechanical ventilation:** The transition from spontaneous to mechanical ventilation invariably produces hemodynamic changes due to acute changes in the intra-thoracic pressure and chest wall compliance. The effects of mechanical ventilation differ according the lesion of the lung:
  - **In obstructive lung disease**, controlled mechanical ventilation magnifies **air-trapping**, producing pulmonary tamponade, which causes **circulatory collapse**; so, the ventilatory pattern should be adjusted accordingly at: **an I: E ratio of ≥ 1: 3 and a moderate tidal volume.**
  - **In restrictive lung disease**, the ventilatory pattern should be adjusted at: **high inflation pressure** and **PEEP**.
  - **In both obstructive and restrictive lung diseases**, optimal balance of ventilation with hemodynamic stability often necessitates tolerating a degree of hypercapnia (it may increase progressively intraoperatively; so, it should be monitored).
  - **In pulmonary hypertension,** avoid factors which increase pulmonary vascular resistance such as hypoxia, hypercarbia, and lung hyperinflation.

Intraoperative Problems:

1) Surgical Technical Differences between Single and Double Lung Transplant:

It is extremely important that anesthesiologists be broadly familiar with the surgical procedures since manipulation of the heart and lungs at specific points during the transplant can produce marked cardiopulmonary disturbances. Therefore, the anesthesiologist can anticipate these changes and adapt the anesthetic management accordingly.

	Single Lung Transplant	Double Lung Transplant
Patient Position	Lateral decubitus	Supine
Skin Incision	Posterior or postero-lateral thoracotomy	**Clamshell incision** i.e., bilateral thoracotomies (antero-thoraco-sternotomy), which extend from the mid-axillary lines to meet in the center via a transverse sternotomy.
Technique In both	• **Intermittent single lung ventilation** is needed during dissection. • **Assess the cardio-pulmonary response** by diverting the entire cardiac output through one lung as **progressive occlusion of the pulmonary vessel is first performed manually**; if well tolerated, the vessel is then clamped and stapled. After ligation of the pulmonary artery, the pneumonectomy is completed.	

	• Implantation of the graft begins with: ▫ anastomosis of **the airway**, then ▫ anastomosis of **the pulmonary artery branch**, which is followed by ▫ anastomosis of **the cuff of the left atrium** containing the pulmonary veins. ▫ Methylprednisolone is usually given before release of the vascular clamp.	
Cardio-Pulmonary Bypass (CPB)	• In absence of severe pulmonary hypertension, it is **usually not needed,** where the ventilation during surgery can be maintained by ventilating the contralateral lung during each implantation. • The need of CPB depends on the patient's response to collapsing the diseased lung and to clamping its pulmonary artery. Some patients develop: ▫ persistent arterial hypoxemia (SPO_2 <90%) and ▫ a sudden increase in pulmonary artery pressure (especially those with pulmonary hypertension) resulting in severe right ventricular dysfunction. Therefore, normothermic CPB is needed. • During left thoracotomy, a femoral vein to femoral artery bypass is used; while during right thoracotomy, a right atrium to aorta bypass is used.	• **In the past**, all cases required **CPB** as both lungs were removed together **"en bloc".** • **Recently**, a bilateral sequential (one after the other) implantation technique is used, which usually does not need CPB where at first, **the most severely compromised lung** (as determined by preoperative ventilation/perfusion scanning) **is removed** and implantation of the 1st lung is done **during ventilation with the good contralateral lung.** Then removal and implantation of the other side are done during **ventilation with the new 1st lung alone.**

2) Effects of Single Lung Ventilation:

a) Hypoxia:

• In a single lung transplant, the patient is in the **lateral position;** so, **gravity helps** redistribute blood away from the non-ventilated non-dependent lung during single lung ventilation. This **decreases the intra-pulmonary shunt**. Therefore, **hypoxia is rarely a problem**.

But in a double lung transplant, the patient is in the supine position so this effect is lost.

• In **severe obstructive lung** diseases, there are **large residual lung volumes** that will be filled with high O_2 concentration during the initial stages of the procedure; so, the patient may initially maintain oxygenation for the first 10-15 minutes of single-lung ventilation, then hypoxia and hypercarbia will occur slowly once the residual volume is absorbed.

In **restrictive lung diseases**, there are **small residual lung volumes,** so the patients rapidly exhibit both hypoxia and hypercarbia.

• Measures to prevent and treat hypoxia (if it occurs) are discussed above.

b) Marked Acute Increase in the Peak Inspiratory Pressure with a subsequent gradual and progressive increase in the Pulmonary Artery Pressure:

• Due to hypoxic pulmonary vasoconstriction (HPV) reflex and blood flow redistribution, there is an increase in the afterload on the right ventricle causing **right ventricular dysfunction** i.e., it becomes hypo-kinetic and distended with decreased ejection fraction; so, close monitoring of right ventricular function is required.

• Management:

1- Reduction of airway pressure.
2- Inotropes as dobutamine or dopamine.
3- Phosphodiesterase inhibitors as amrinone or milrinone.
4- Pulmonary vasodilators as prostaglandins E_1, nitroglycerin (given before initiation of OLV).
5- CPB and heparinization if persistent right ventricular dysfunction, hypoxia, or hypercarbia is present.

N.B.: Effect of Clamping of the Pulmonary Artery:

It is discussed in OLV (see above). In most patients undergoing single lung transplant, hypoxia during OLV and pulmonary artery clamping is rarely a problem.

3) Changes during Graft Reperfusion:

a) **Decreased pulmonary artery pressure: Usually** after reperfusion and subsequent ventilation of the new lung, fall of the pulmonary artery pressure occurs. Sometimes, on reperfusion of the first lung, a rapid progressive **increase in the pulmonary artery** pressure occurs with increased inspiratory pressure,

hypoxia, hypotension, and pulmonary edema. This needs adjustment of the ventilation, PEEP, and pharmacological support. If these measures fail, CPB is required.

b) If the graft is reperfused after a **lengthy ischemia, tissue damage of the graft** may occur.

c) **Hyperkalemia** may occur as the preservative fluid (such as Euro–Collins) is washed out of the donor organ.

d) Ventilation is resumed in both lungs (after the procedure) with keeping:
- the peak inspiratory pressure to the minimum pressure compatible with good lung expansion and
- $FiO_2 < 60\%$.

e) **Transient hypotension** due to the introduction of vasodilator-containing lung graft preservatives into the systemic circulation.

f) **Transient myocardial ischemia** due to incomplete de-airing of the lung. It can cause coronary air embolism.

g) **Early graft dysfunction** may occur. It ranges in severity from the mildest chest x-ray abnormalities to fulminant pulmonary edema with hypoxia and cardio-vascular compromise. It needs immediate adjustment of ventilation, PEEP, pulmonary vasodilators, inhalation of nitric oxide, and initiation of CPB.

4) Intraoperative Fluid Management:

Generally, the amounts of intraoperative fluids should be kept to a **minimum** although:
- **Many patients require large amounts of fluids** (crystalloids and colloids) to maintain hemodynamic stability.
- **Central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) of 3-5 mm Hg** usually occur immediately after the transplant in spite of infusion of large amounts of fluids and only moderate blood loss.

Extubation:

- Patients are usually **left intubated** for **24-72 hours** where **the double-lumen tube is changed with an ordinary endotracheal lumen** (with the help of an exchange catheter with care not to advance the catheter too far and damage the graft).
- **Fiberoptic bronchoscopy** is performed after tube changing to:
  - examine bronchial anastomosis and
  - aggressively suction secretions or blood.
- **This delayed extubation** is due to:
  - The cardio-pulmonary insult associated with the procedure.
  - Large postoperative volume shifts.
  - Hypothermia.
  - Frequent need for postoperative bronchoscopy.
- **The double lumen tube is left in place and not exchanged in case of:**
  - Intraoperative events (such as hyper-inflation of the remaining intact lung), which require **post-operative differential lung ventilation**.
  - **Profound oropharyngeal edema.**
  - **Difficult intubation.**

Postoperative Management and Intensive Care Considerations

1- Postoperative Ventilation:

- Most patients are weaned from ventilation (with decreased FiO_2) and extubated as soon as the patient is warm and stable. In patients who have undergone single lung transplant for pulmonary hypertension, the tube is usually left for 48-72 hours postoperatively due to a great possibility of cardio-pulmonary instability during the 1st 48-72 hours.
- **Postoperative pulmonary function tests (ventilation/perfusion matching)** are:
  - **worse after single** lung transplant **than bilateral** lung transplant and
  - different after single lung transplant, according to the original disease process:
    - In **obstructive** lung diseases, pulmonary function tests are **worse** because the remaining native lung often receives a considerable portion of the tidal volume.
    - In **restrictive** lung diseases, pulmonary function tests are better because the graft receives the majority of both the ventilation and perfusion.
    - In patients with **pulmonary hypertension**, pulmonary function tests are **the worst** because the remaining native lung continues to be ventilated but receives minimal blood flow.

N.B.: Pulmonary function tests improve with the transplanted side up in obstructive and pulmonary hypertension while improve with the native lung up in restrictive lung diseases due to an unknown cause, but may be due to positional variation in ventilation/perfusion matching.

2) Postoperative Analgesia:

A thoracic or lumbar epidural catheter is used if coagulation studies are normal.

3) Postoperative Complications:

a) Early Complications:

- **Pulmonary edema:** It is usually mild, but in some patients, it is severe, which may cause acute respiratory failure termed **primary graft failure.** The diagnosis is confirmed by infiltrates seen on chest radiographs and severe hypoxemia during the first 72 hours postoperatively. Treatment is supportive and includes mechanical ventilation.
- **Bleeding.**
- **Technical problems** with vascular or bronchial anastomosis such as:
  - dehiscence of the anastomosis (which mandates immediate surgical correction or re-transplantation).
  - airway stenosis (which causes focal wheezing, recurrent lower respiratory tract infection and sub-optimal pulmonary function).
- **Profound reperfusion injury** resulting in graft failure, which necessitates re-transplantation.
- **Acute rejection:** is usually seen during **the first 100 days following transplantation**. It is manifested by nonspecific clinical picture such as malaise, low-grade fever, dyspnea, impaired oxygenation, and leukocytosis. Frequent bronchoscopy **with trans-bronchial lung biopsies and lavage** are needed to differentiate between rejection and infection. Treatment includes i.v. methylprednisolone. Graft failure may require temporary extracorporeal membrane oxygenation.
- **Surgical complications** such as **injury to the phrenic, vagus, or left recurrent laryngeal nerve.**

b) Delayed Complications:

- **Infection**: The most common cause of death in ≤ 90 days after surgery by nosocomial gram-negative bacteria, cytomegalovirus, candida, aspergillus, and pneumocystis carinii.
- **Chronic rejection**: It is manifested by **bronchiolitis obliterans** where there is small airway fibrosis and obliteration. It is characterized by dyspnea, cough, repeated infections. It is the most common cause of death in > 90 days of surgery. Chronic rejection requires re-transplantation.
- **Malignancy.**

N.B.: Multiple fiberoptic and/or rigid bronchoscopic procedures are common because many patients require tracheal/bronchial dilatation, laser therapy, or endobronchial stent placement.

N.B.: The most common causes of death (arranged in order):

a- Within 90 days after surgery:
- Non-cytomegalovirus infection.
- Primary organ failure.
- Heart Failure.
- Hemorrhage.

b- After 90 days:
- Bronchiolitis obliterans/chronic rejection.
- Non-cytomegalovirus infection.
- Malignancy.
- Respiratory failure.

Surgical Alternatives to Lung Transplantation

Lung Volume Reduction Surgery (Reduction Pneumoplasty)

Indication:

Reduction Pneumoplasty is indicated in selected patients with severe emphysema who are not candidates for lung transplants.

Aim:

- To **remove up to 30% of the patient's most severely compromised lung tissue** allowing the patient's previously hyper-expanded chest wall and depressed diaphragm to resume a more normal shape and allowing normal areas of the lung to be more expanding. This **improves chest wall mechanics** and

improves pulmonary function. This beneficial effect requires 1-2 months postoperatively to become apparent.

Anesthetic Considerations:

- Preoperative assessment of chronic obstructive airway disease is essential. It is discussed in details in chapter "Respiratory Disease".
- OLV is needed.
- Both N_2O and excessive positive airway pressure should be avoided.
- A median sternotomy or bilateral thoracoscopies may be required, which need very good postoperative analgesia.
- Postoperative pulmonary complications may occur. It is discussed in the chapter of "Respiratory Diseases".

Anesthesia for a Patient with a Transplanted Lung

Physiological Effects of after Lung Transplantation:

1- Loss of neural connections (a denervated lung): results in

- **Loss of the cough reflex and impairment of mucociliary clearance (below the anastomosis)** during the early postoperative period due to disrupted innervation of the lung, which places patients at risk of aspiration and pulmonary infection.
- **Bronchial hyperactivity** in some patients.
- **A blunted ventilatory response to CO_2 and hypercarbia with increased sensitivity to opioids**, which persists even though pulmonary function improves.

In the same time, **the following items are not affected**:

- **The respiratory pattern** is not affected. It is mainly under control of central respiratory centers, which control the diaphragm and accessory muscles.
- **Hypoxic pulmonary vasoconstriction** reflex remains normal, which is due to local mechanisms.
- **Oxygenation:** Peak improvement is usually achieved within 3 to 6 months. Arterial oxygenation rapidly returns to normal, and supplemental oxygen is no longer needed.
- **Exercise capacity:** improves sufficiently to permit most lung transplant patients to resume an active lifestyle.

2- Loss of lymphatic drainage: results in

- Increased extra-vascular lung water which predisposes **to pulmonary edema** of the transplanted lung; therefore, **intraoperative and postoperative fluid** replacement must be kept to a **minimum.**
- The lymphatic drainage is then re-established 2-4 weeks post-transplantation.

3- Loss of bronchial circulation: results in

- Predisposition to **ischemic breakdown** of the bronchial suture line.

4- Pulmonary vascular resistance and pulmonary artery pressure: In patients with a pulmonary vascular disease, both single and bilateral lung transplantation result in immediate and sustained normalization of pulmonary vascular resistance and pulmonary artery pressure. This is accompanied by a prompt **increase in cardiac output** and **gradual remodeling of the right ventricle** with a decrease in ventricular wall thickness.

5- Denervation of the heart: is another consideration in patients undergoing **heart-lung transplantation or** even in some patients undergoing **double lung transplantation**. It is discussed in details in the chapter of "Cardiac Surgery".

Anesthetic Considerations

Preoperative Considerations:

- Preoperative assessment of the **pulmonary function** is essential e.g., history, pulmonary function tests, arterial blood gases, chest radiographs…etc.
- Assessment for the **side effects of immunosuppressive drugs** is important e.g., hypertension, renal dysfunction of cyclosporine…etc. in addition to the **complete aseptic techniques** e.g., during insertion of central lines and **prophylactic antibiotics** required.
- **Supplemental corticosteroids** may be needed for long stressful surgical procedures.

Intraoperative Considerations:

- **Monitors:**
  - If **central venous catheter** is inserted via the internal jugular vein, it is prudent to select the internal jugular vein **on the side of the native lung**.
  - **Differences** in the compliance and expiratory flow rates of **a native and transplanted lung** after single lung transplant for emphysema cause alterations in **intraoperative capnography;** so, **a biphasic pattern** of CO_2 exhalation is produced, with the first peak reflecting exhalation from the transplanted lung, and the second peak exhalation from the native lung.
  - **In heart-lung transplant recipients,** fluid management may be a particular challenge because the **cardiac output is preload dependent** i.e., adequate fluid is required, but the lungs have a **higher possibility to develop pulmonary edema**, especially in the first 2-4 weeks post-transplantation. Therefore, **invasive monitoring** is very important with great care for the risk of infection. **Trans-esophageal echocardiography** is very helpful to monitor the volume status and cardiac function without risk of infection.
- **Regional anesthesia is recommended** whenever possible because these patients cannot clear their airways except if they are awake due to loss and decrease of cough reflex. Epidural and spinal anesthesia are acceptable, but **avoid depression of intercostal muscle function. Care of infection** is very important especially during performing regional anesthesia. **Fluid preloading** before a spinal or epidural block may be **risky** in patients with a transplanted lung because disruption of the lymphatic drainage causes **interstitial pulmonary edema.**
- The position of **the endotracheal tube's cuff** should be **just beyond the vocal cords** to minimize the risk of traumatizing the tracheal anastomosis. If **a double-lumen tube** is required, it is preferable to place the endo-bronchial portion of the tube **in the native bronchus** under direct vision using a fiberscope, thus avoiding contact with the tracheal anastomosis.
- There is **increased sensitivity to opioids.**

Postoperative Considerations:

- Search for **postoperative complications after lung transplantation** especially bronchiolitis obliterans (chronic rejection).

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NEUROMUSCULAR DISEASES

27

- Neuromuscular disorders
- Myasthenia gravis
- Myasthenic syndrome (Eaton-Lambert syndrome)
- Muscular dystrophies
- Myotonia
- Familial periodic paralysis
- Botulism
- Critical care neuromuscular disorders (critical illness polyneuropathy and myopathy)
- Channelopathies

Neuromuscular Disorders

They are classified into:

1) Motor Cortex and Pyramidal Tract (Upper Motor Neuron):

- Amyotrophic lateral sclerosis.
- Multiple sclerosis.

2) Brain Stem:

- Progressive bulbar palsy.

3) Spinal Cord and Lower Motor Neuron (Denervation Disorders):

- Spinal muscular atrophies.
- Amyotrophic lateral sclerosis.
- Syringomyelia.
- Poliomyelitis.
- Infections: tetanus, spinal cord and epidural abscesses.
- Spinal cord trauma.
- Toxins: mercury.

4) Peripheral Neuropathies:

- Axonal Types (as critical illness polyneuropathy).
- Alcohol- related.
- Hypothyroidism.
- Collagen vascular disease.
- Amyloidosis.
- Guillain-Barré syndrome.
- Porphyria.
- Drugs: anticonvulsant therapy.
- Tick paralysis.
- Diabetes.
- Uremia.
- Sarcoidosis.
- Paraproteinemia.
- Carcinoma (remote effect).
- Diphtheria.
- Demyelinating neuropathies.
- Toxins: industrial toxins and heavy metals.
- Hereditary: Charcot-Marie-tooth disease.

5) Neuromuscular Junction Disorders:

- Myasthenia gravis (postsynaptic).
- Botulism (presynaptic).
- Psuedo-cholinesterase deficiency or abnormalities.
- Eaton-Lambert syndrome.
- Drugs: neomycin, penicillamine.
- Toxins: organophosphate toxicity.

6) Diseases of Muscles: (postsynaptic)

- Muscular dystrophies as Duchenne's dystrophy.
- Inflammatory myopathies.
- Neuroleptic malignant syndrome.
- Myotonia.
- Toxic myopathies: alcohol, carbon monoxide.
- Malignant hyperthermia.
- Inherited metabolic myopathies: familial periodic paralysis, glycogen or lipid enzymatic defect.
- Endocrine and metabolic myopathies as thyrotoxicosis, myxedema.
- Drugs: prolonged steroid therapy and non-depolarizing blockade.

Myasthenia Gravis

Incidence: 1: 30 000. 2/3 of cases are **women.**

Cause: **Autoimmune destruction** or inactivation of **postsynaptic nicotinic acetylcholine receptors** at the neuromuscular junction (NMJ) by **antibodies** produced from T-cells of the thymus gland.

Clinical Picture:

A) Adult Type:

The onset occurs in **females** in the **3rd decade** and in **males** in the **6th–7th decade**.

Course: Exacerbations and remissions evoked by infections, stress, surgery, pregnancy, and drugs as aminoglycosides, ciprofloxacin, colistin, polymyxin, quinidine, procainamide, lignocaine, penicillamine, phenytoin, lithium, beta-blockers, magnesium, and respiratory depressants.

The weakness of skeletal muscles is characterized by:

- **Asymmetric** affection.
- The deficit in myasthenia is purely motor (when up to 80% of functional receptors are lost) with **no sensory involvement.**
- **Painless weakness** occurs in a **descending manner:**
  - **The eye muscles** are the first affected muscle resulting in:
    - **Ptosis** (the most common complaint) that is either uni- or bilateral, symmetric or asymmetric, and alternates between eyes.
    - **Diplopia** (the 2nd most common complaint).
  - Then **bulbar muscles** are affected e.g. laryngeal and pharyngeal muscles resulting in dysarthria, dysphagia, problems of clearing secretions or pulmonary aspirations, nasal toned voice indicating palatal paralysis.
  - **Facial muscles** are then affected especially elevators of the angles of the mouth resulting in the characteristic **"Myasthenia Snarl"**.
  - **Neck muscles.**
  - **Respiratory muscles.**
  - **Limb girdle muscles**; proximal then distal limb muscles.
  - **Trunk muscles** are affected lastly.
- The weakness **improves by rest** and **worsens by repeated effort and exercise** and at the end of the day.
- **Myasthenic crisis:** occurs when rapid progression to respiratory failure and ventilator dependence occur. It occurs in 15-20% of patients.

Associated Autoimmune Disorders:

- Hypo- or hyperthyroidism.
- Rheumatoid arthritis and systemic lupus erythematosis.
- Myocarditis resulting in cardiomyopathy, atrial fibrillation, or heart block.
- Thymic enlargement: thymoma in 10% of cases and thymic hyperplasia in 70% of the cases.

B) Juvenile Type:

It occurs before **2 years of age.** It is confined to **bulbar muscles.**

C) Neonatal Type:

It occurs in **babies of myasthenic mothers** who may show transient myasthenia for 1- 3 weeks and may need mechanical ventilation due to placental transfer of antibodies.

Another Classification (by Osserman and Genkins):

Class I: ocular muscle weakness.
Class II: mild non-ocular muscle weakness (sparing respiratory muscles).
Class III: moderate non-ocular muscle weakness.
Class IV: severe non-ocular muscle weakness.
Class V: Tracheal intubation (except in the perioperative period) or tracheostomy to protect the airway with or without mechanical ventilation.

Differential Diagnosis:

1- Myasthenic crisis and cholinergic crisis: Both are muscle weakness emergencies. Cholinergic crisis may occur by toxicity of anticholinesterase drugs used in treatment of myasthenia gravis.

	Myasthenic Crisis	Cholinergic Crisis
Cause	Exacerbation of myasthenia due to inadequate treatment, drug-induced infection…etc.	Excessive anticholinesterase treatment.
Edrophonium test	Improvement occurs.	Worsening occurs.
Muscarinic symptoms	Absent e.g., pupil diameter is > 3 mm	Present e.g., miosis, salivation, bradycardia, diarrhea, sweating…etc.
Treatment	• Anticholinesterase with atropine. • Mechanical ventilation. • Antibiotics for infection. • Plasmapheresis.	• Stop anticholinesterase and give atropine. • Mechanical ventilation. • Pralidoxime (PAM) 500 mg i.v. infusion.

2- Myasthenic syndrome (Eaton- Lambert syndrome).

3- Other diseases producing muscle weakness e.g., thyrotoxicosis, neurasthenia, progressive external ophthalmoplegia muscular dystrophies, brain tumors, and amyotrophic lateral sclerosis.

Investigations:

A- Electrophysiological Tests:

1. Peripheral Nerve Stimulator:

Electromyography shows a **rapid decrease in the amplitude** of the compound action potential evoked during **repetitive stimulation** of a peripheral nerve (usually the circumflex humoral, median, or ulnar nerves) by supra-maximal stimulation of 2-3 Hz, four times over 2 sec, in a train of four patterns. The twitch response is decreased 10% when the 4th response is compared to the 1st. This is diagnostic of myasthenia gravis. Also, minimal post-tetanic facilitation is present. **The sensitivity** of this test is **50-70%**. Diseases affecting the presynaptic nerve terminal such as Eaton-Lambert syndrome or botulism demonstrate an incremental response at a higher rate of stimulation.

2. Single Fiber Electromyography:

It evaluates the time interval between 2 muscle fiber action potentials in the same motor unit. As the same nerve innervates both muscle fibers, the time variation between their action potentials, known as the **"jitter"**, is a manifestation of NMJ transmission. In patients with myasthenia gravis, the jitter is increased. **It is a > 90% sensitive test** although it is **not specific for myasthenia gravis**.

3. Stapedius reflexometry.

4. Nystagraphy.

B- Pharmacological Tests:

Edrophonium Test: It is performed as follows:

- Stop other anticholinesterase medications 24 hours prior to the test if possible.
- Atropine sulfate 0.4 mg should be given to block muscarinic side effects of edrophonium but not the nicotinic effect at the neuromuscular junction.
- Edrophonium (*Tensilon*) 2 mg are given at first; if there is no response, follow with 8 mg. A response should occur in 30-60 seconds that should last for 10-30 minutes. The strength of the affected muscles should be assessed 1-2 minutes after each i.v. dose. A dramatically improved response should occur.

C- Serological Tests:

Detection of Antibodies: They are present in patient's serum in 80-95% of cases. The absence of acetylcholine receptor antibodies does not exclude the diagnosis, but their presence is confirmatory.

D- Imaging Studies:

Chest CT scan or MRI can detect thymoma in 10% of cases or thymic hyperplasia in 70% of cases.

Treatment:

1- Anticholinesterase Drugs:

It inhibits breakdown of acetylcholine by tissue cholinesterases resulting in an increase of acetylcholine at neuromuscular junction. For example:

- **Pyridostigmine** *(Mestinone)*: It produces less muscarinic effects.

Dose: 60-120 mg oral every 4-6 hours or
2 mg i.v./i.m. every 6 hours.

- **Neostigmine** *(Prostigmine)*: It produces greater muscarinic effects.

Dose: 15 mg oral every 6 hours,
1.5 mg i.m. every 6 hours, or
0.5 mg i.v. every 6 hours.

Atropine or propantheline are vagolytic drugs, which should be given with anticholinesterase to block muscarinic effects.

2- Immunosuppressive Drugs: are used to decrease antibody production. They are used in severe cases. For example:
- Corticosteroids as prednisolone 10 mg/day (it is used with anti-cholinesterases).
- Methotrexate.
- Cyclophosphamide.
- Azathioprine.

3- Plasmapheresis:
It is used to **remove antibodies** as an emergency treatment or during preoperative preparation. 2-3 liters exchange, 3 times a week over 2 weeks, has been successful in some patients who do not respond to anticholinesterase medications. In other cases, there is unpredictable response.

4- I.v. Immunoglobulin:
It is an alternative to plasmapheresis, and can be used also in preparing patients for thymectomy.

5- Thymectomy:
It is mainly indicated for patients < 40 years old with thymoma. Improvement occurs in 50% of patients.

Anesthetic Management:

Preoperative Management:

1- Preoperative Assessment of Muscle Weakness: such as:
- **Bulbar muscle** weakness causes problems of clearing secretions or **pulmonary aspiration.**
- **Respiratory muscle affection** causes **difficult breathing.**
- **Edrophonium test** may be done to exclude cholinergic crisis.
- **Preoperative predictive criteria for postoperative need for mechanical ventilation are assessed.** A scoring system is assigned by Leventhal, Orkin, and Hirsch as follows:

Description	Points
Duration of the disease > 6 years	12
History of chronic respiratory disease	10
Pyridostigmine dose > 750 mg/day (in the day before surgery)	8
Preoperative vital capacity < 2.9 liters	4

Patients with a score **< 10 points**, could be **extubated** immediately postoperatively.
Patients with a score **> 12 points,** need **postoperative ventilation.**
This scoring system is not universally applicable for all patients.

2- Preoperative Assessment of Associated Autoimmune Diseases:
Such as hypo- or hyperthyroidism, rheumatoid arthritis, systemic lupus erythematosis, myocarditis, and thymic enlargement.

3- Preoperative Investigations:
Besides the standard investigations required,
serum electrolytes (e.g., hypokalemia potentiates myasthenia gravis),
arterial blood gases, and
pulmonary function tests.

4- Preoperative Treatment of myasthenia gravis as above.
The use of anticholinesterases is **controversial** because they produce:
- **Increased vagal effects,** which ▫ increase bronchial secretions and bronchospasm,
  ▫ induce bradycardia, and
  ▫ increase peristaltic movement.
- **Inhibition of plasma cholinesterase** enzymes prolongs the action of the ester type of local anesthetics, succinylcholine, and mivacurium.

Conversely, patients with a severe form of the disease may **deteriorate more on stopping anticholinesterases.**
Therefore, it is recommended that for:
- Patients with a **severe form** of the disease and dependent on anticholinesterase, **only decrease the dose preoperatively.**
- Patients with a **mild form** of the disease and dependent on anticholinesterase, **stop the drug, even if 4 hours preoperatively.**

5- Premedications:

1- Sedatives: Decrease the dose as there is increased sensitivity to respiratory depressant drugs.
2- Aspiration prophylaxis: as antacids, H_2 blockers, and metoclopramide.
3- Antisialagogue: Atropine i.m. 1 hour before the surgery.
4- Steroid cover: if the patient was on steroid therapy.

Intraoperative Management:

Monitoring: Besides the standard monitors,

- Invasive blood pressure (and arterial blood gases): if there is a possibility of intra-thoracic procedures or postoperative ventilation.
- Peripheral nerve stimulator: to adjust the dose of muscle relaxants.

Choice of Anesthesia:

a- Regional or Local Anesthesia:

It is preferred, but with the following precautions:

1- Decrease the dose of local anesthetics due to:

- their neuromuscular blocking actions.
- prolonged action of **ester local anesthetics** due to inhibition of plasma cholinesterases by anticholinesterase therapy.

2- Avoid high level blocks as they may cause hypoventilation.

Advantages: • Avoids the use of muscle relaxants.
• Avoids loss of consciousness; so, decreases the risk of aspiration.

b- General Anesthesia:

As a rule:

- Avoid the use of muscle relaxants as much as possible because they may cause an unpredictable response.
- If a muscle relaxant is mandatory, use a short-acting muscle relaxant in the smallest possible dose with a nerve stimulator.

Induction:

Thiopentone or ketamine i.v. can be used in a small dose due to possibility of respiratory depression.
No opioids are used due to their respiratory depression.

Intubation:

Deep volatile anesthesia is used as it produces sufficient muscle relaxation for intubation.
Succinylcholine should be avoided and if used it should be with the smallest possible dose because:

- It causes an **unpredictable** response. It may show resistance (due to an unknown mechanism or due to decreased number of acetylcholine receptors). Phase II block may also occur with a single intubating dose.
- Patients treated with anticholinesterase may show prolonged response to succinylcholine because anticholinesterases may also inhibit plasma cholinesterases.

Maintenance:

$O_2 + N_2O$ + Volatile agent-based anesthesia

- **Deep volatile anesthesia** allows good muscle relaxation. This decreases the dose or eliminates the need for intraoperative muscle relaxants, because myasthenia gravis patients are very sensitive to the relaxant effects of volatile agents.
- **Avoid non-depolarizing muscle relaxants (even in defasciculation doses)**, because the decreased acetylcholine receptors (up to 70%) cause a very sensitive response. If muscle relaxants are necessary in major surgeries requiring muscle relaxation,
  - Use a small dose (10-20% the normal).
  - Use short and intermediate acting agents e.g., atracurium or vecuronium (N.B.: mivacurium is not suitable for use because it is metabolized by plasma cholinesterase).
  - A peripheral nerve stimulator is essential.
  - Anticholinesterases should be stopped for 4 hours before surgery because they may interfere with the action of the non-depolarizing muscle relaxants.

N.B.: Corticosteroids cause resistance to steroidal non-depolarizing muscle relaxants e.g., vecuronium, but have no effect on suxamethonium.

- Avoid opioids as they produce marked respiratory depression because myasthenia gravis patients are very sensitive to their respiratory depressant effect.

Recovery:

Extubation occurs after:

1. Assessment of the ventilatory function e.g., patient can create a good negative inspiratory force (of at least - 20 cm H_2O).
2. Good muscle power has returned, detected by using a nerve stimulator.

Postoperative Management:

1- **Elective postoperative ventilation** for 24-48 hours postoperatively may be needed for patients with preoperative predictive criteria (see before).

2- **Chest physiotherapy and tracheal suction**.

3- **Postoperative analgesia:**

- Epidural opioids are safer.
- If parenteral opioids are used, they should be used at the minimal dose possible.

4- **Postoperative complications:**

Exacerbation of weakness whether due to a myasthenic or cholinergic crisis, should be differentiated.

Myasthenic Syndrome (Eaton-Lambert Syndrome)

It is an autoimmune disease due to antibody production against presynaptic Ca^{++} channels.

Differential diagnosis: Myasthenia gravis.

	Myasthenia Gravis	Myasthenic Syndrome
Muscle Weakness	• In extraocular muscles, bulbar muscles, neck muscles…etc. • Increased by repeated efforts. • Muscle pain is uncommon. • Reflexes are normal. • More in females.	• **In proximal limb muscles**. • **Decreased by repeated efforts.** • **Muscle pain** is common. • **Reflexes are depressed or absent.** • More in **males**.
Coexisting Diseases	• Autoimmune diseases as thymoma…etc.	• Small cell carcinoma of lung.
Response to Muscle Relaxants	• Resistant (or variable response) to suxamethonium. • Sensitive to non-depolarizing muscle relaxants. • Good response to anticholinesterases.	• Sensitive to suxamethonium and sensitive to non-depolarizing muscle relaxants. • Poor response to anti-cholinesterases.
Electro-myographic Response	• Voltage decrement to repeated stimulation.	• Voltage increment to repeated stimulation.
Autonomic Nervous System Abnormality	• Not present.	• Present.
Treatment	• Anticholinesterases, steroids, plasma-pheresis, azathioprine, and thymectomy.	• Steroids, plasma-pheresis, azathioprine, guanidine and 3,4-di-aminopyridine (they cause acetylcholine release).

Muscular Dystrophies

They are a group of disorders characterized by painless degeneration and atrophy of skeletal muscles, with a normal sensory system. They are classified according to inheritance:

- **X-linked:** ▫ Duchenne's muscular dystrophy.
  ▫ Becker's muscular dystrophy.
- **Autosomal dominant:** ▫ Facio-scapulo-humoral dystrophy.
  ▫ Oculo-pharyngeal dystrophy.
  ▫ Nemaline rod muscular dystrophy.
  ▫ Myotonic muscular dystrophy.
- **Autosomal recessive:** ▫ Limb-girdle dystrophy (Landouzy-Dejerine).
  ▫ Childhood dystrophy.
  ▫ Congenital dystrophy.

1) Duchenne's Muscular Dystrophy and Becker's Muscular Dystrophy

It is **an X- linked** recessive disease, affecting males.
- Duchenne's syndrome affects males at 3-5 years old.
- Becker's syndrome affects male adolescents.

In these conditions, α-dystroglycan dysglycosylation is the most common pathophysiology for congenital muscular dystrophies. There is a defect (deletion or duplication) in dystrophin (a protein found on the sclerolemma of muscle fibers).

Investigations:

1- An **increase in plasma creatine kinase (CK) levels**, from 10-100 times (due to a defect in the permeability of muscle cell membranes).
2- **Increased plasma myoglobin** concentration.
3- **Muscle biopsy** is diagnostic as it shows progressive muscle fiber necrosis.
4- Detection of a defect (deletion or duplication) in dystrophin by Southern blot analysis or polymerase chain reaction methods in 56% of patients.

Anesthetic Problems (and Clinical Picture):

It is the same for both Duchenne's and Becker's syndrome except for age.

- Skeletal muscle affection:
  - Proximal symmetrical weakness causes gait disturbances (waddling gait) and **increased incidence of bone fracture;** so, care is taken during positioning.
  - Fatty infiltration of calf muscles (gastrocnemius muscles) resulting in **pseudo-hypertrophy**.
  - **Malignant hyperthermia** may occur. Dantrolene should be available.
- Respiratory muscle affection:
  - There is degeneration of the muscles, which interferes with cough and causes **retention of secretions**, and repeated **chest infections** (a cause of death)
  - **Restrictive lung disease (kyphoscoliosis) and pulmonary hypertension** are common.
- Cardiac muscle affection:
  - Degeneration of the muscle may result in **dilated cardiomyopathy** (a cause of death); therefore, marked myocardial depression may occur with **volatile agents**. **Opioids are better** tolerated.
  - Papillary muscle dysfunction may occur resulting in **mitral regurgitation.**
  - **ECG changes** are common (a tall R wave in V_1 and deep Q wave in limb leads, with a short PR interval, and increased heart rate).
- Gastrointestinal muscle affection:
  - Decreased motility is present which increases the **risk of aspiration**; therefore, premedication with opioids and sedatives should be avoided.

Anesthetic Techniques:

- **Regional anesthesia is preferred**.
- **Avoid succinylcholine** because
  - it produces unpredictable response,
  - it induces severe hyperkalemia, which causes ventricular fibrillation.
  - it may trigger malignant hyperthermia.
- **Avoid non-depolarizing muscle relaxants** due to their unpredictable responses.

2) Facio-Scapulo-Humeral Dystrophy

It is autosomal dominant affecting males and females at ages around 20-30 years old.
Weakness of muscles affects mainly the muscles of the face and shoulders.

3) Oculo-Pharyngeal Dystrophy

It is autosomal dominant affecting males and females.
It is associated with Ptosis and dysphagia resulting in risk of aspiration.

4) Nemaline Rod Muscular Dystrophy

It is autosomal dominant affecting males and females at infancy.
Progressive symmetric skeletal muscle weakness is usually present with hypotonia, dysphagia, and respiratory distress which results in cyanosis.
It is associated with anomalies such as micrognathia (resulting in difficult intubation), kyphoscoliosis (resulting in restrictive lung disease), and associated with congestive heart failure and bulbar palsy (resulting in regurgitation and aspiration).

5) Myotonic Muscular Dystrophy

It is sometimes considered as a separate entity called myotonia. It is discussed later.

6) Limb-Girdle Dystrophy (Landouzy- Dejerine)

It is autosomal recessive affecting males and females at ages around 20-30 years old.
It produces weakness of shoulder muscles (Erb's type) or hip girdle muscles (Leyden-Möbius type). There is usually cardiac affection.

Anesthetic Problems: types from (2) up to (6).
They show normal response to anesthetic agents, but due to the overlap of the different types, it would be **better to avoid suxamethonium and non-depolarizing muscle relaxants.**

Myotonia

- Myotonia means increased muscle tone. **There are sustained contractions** of muscles after voluntary or mechanical stimulation, which **fail to relax** after the use of non-depolarizing muscle relaxants, general anesthesia, or regional anesthesia. The myotonia is usually described by patients as a "stiffness" that may ease with continued activity, the so-called **"warm-up" phenomenon.**
- They can **relax after** the use of **local anesthetic injection in the contracting muscles** such as procaine, due to **abnormal Ca^{++} metabolism**. The cellular ATP system **fails to return Ca^{++} into the sarcoplasmic reticulum.**
- Antimyotonic treatment with a membrane stabilizing action can be used such as phenytoin, quinine sulfate, and procainamide.
- Myotonia includes myotonic muscular dystrophy, myotonia congenita, and para-myotonia congenita.

1- Myotonic Muscular Dystrophy (Dystrophica Myotonica or Myotonia Atrophica)

It is autosomal dominant disease due to a defect in a gene located on chromosome 19. It affects males and females at ages around 20-30 years old.

Anesthetic Problems (and Clinical Picture):

- Skeletal muscle affection:
  - Muscle spasm is evoked by succinylcholine and anticholinesterases such as neostigmine and physostigmine. They should be avoided because:
    - **they may prevent mouth opening for intubation (trismus).**
    - **there is difficult ventilation** due to respiratory, chest wall, and laryngeal muscle spasm.
  - **Distal muscles** are more involved than proximal muscles (unlike most other myopathies).
  - **Postoperative shivering** (associated with volatile agents) can induce myotonic contractions in the recovery room; therefore, avoid shivering by **a small dose of meperidine**.

Therefore, general anesthesia should be avoided if possible, but regional anesthesia, which is more preferred, cannot prevent myotonic contractions.

- Respiratory muscle affection:
  - There is a decrease in the vital capacity.
  - **Hyper-somnolence with sleep apnea** is common.
  There may be increased sensitivity to even small doses of opioids, sedatives, barbiturates, inhalational or intravenous agents with production of prolonged apnea and respiratory depression.
  - Chronic hypoxia results in **corpulmonale**.
  - **Elective postoperative mechanical ventilation** may be needed.
- Cardiac muscle affection:
  - Heart block, arrhythmias, cardiomyopathy, and congestive heart failure are common; therefore, **avoid** cardiac depression caused by **volatile agents**.
- Gastrointestinal muscle affection:
  - Decreased motility increases **pulmonary aspiration**. Prophylaxis against aspiration should be taken and premedications with opioids and sedatives should be avoided.
- Uterine muscle affection:
  - **Atony** is common during labor, which **prolongs labor and increases uterine bleeding**.
- Facial muscle affection:
  - Weakness of facial muscles (orbicularis oculi and oris, masseter, and sterno-cleidomastoid) results in expressionless facies, ptosis, and dysarthria (a typical facial appearance).

- Other associated clinical pictures:
  - Endocrine: **Insufficiency of pancreatic, adrenal, thyroid, and gonadal functions,** which need to be assessed and managed.
  - Mental retardation.
  - Presenile cataract.
  - Premature frontal boldness.

Avoid non-depolarizing muscle relaxants because:

There is an increased sensitivity to them. Short-acting non-depolarizing agents (as cisatracurium or mivacurium) are recommended.

Reversal by anticholinesterases (as neostigmine) can evoke muscle spasm by facilitating depolarization of the neuromuscular junction.

2- Myotonia Congenita

It is autosomal dominant (Thomson's disease) or autosomal recessive (Becker's disease) appearing early in life. It affects **skeletal muscles** only, where muscle stiffness resolves with exercise.

3- Para-Myotonia Congenita

It is the same as myotonia congenita except muscle weakness occurs **after exposure to coldness**; therefore, avoid decreasing ambient room temperature. It is associated with hyperkalemia.

Familial Periodic Paralysis

It is a condition that shows a sudden attack of transient muscle weakness or paralysis lasting hours or days. The respiratory muscles are spared and are usually not affected.

Anesthetic Problems: It is of three types: hypo-, normo-, or hyperkalemic.

	Hypokalemic Type (Voltage-gated Ca^{++} Channelopathy)	Hyperkalemic Type (Na^{+} Channelopathy)
Incidence	• Common.	• Rare
Pathology	• It is due to voltage-gated Ca^{++} Channelopathy.	• It is due to Na^{+} Channelopathy.
Serum Potassium	• It is < 3.0 mEq/L during the clinical presentation. Repeated serum K^{+} monitoring is needed.	• It is > 5.5 mEq/L during the clinical presentation. Repeated serum K^{+} monitoring is needed.
Avoid	• **Glucose** solutions (and large carbohydrate diets) as they increase K^{+} uptake by cells inducing paralysis. • **K^{+} losing diuretics** (mannitol is used instead if diuretics are needed).	• **K^{+}** containing solutions. • **K^{+} releasing drugs** e.g., succinylcholine.
Give	• **KCl** i.v. slowly with ECG monitoring for preoperative treatment.	• **Glucose infusion** for preoperative treatment. • **K^{+} losing diuretics.** • **Ca^{++}** i.v. for hyperkalemia.

In the 3 types: Muscle relaxants are used cautiously as they may cause an unpredictable response.

Critical Care Neuromuscular Disorders (Critical Illness Polyneuropathy and Myopathy)

Neuromuscular disorders in the critically ill patients are usually associated with progressive and uncontrolled systemic inflammations such as systemic inflammatory response syndrome (SIRS), severe sepsis, and multiple organ dysfunction syndrome (MODS). It is present in 50-70% of critically ill patients.

Causes: The actual cause is still unknown.

- **Drug therapy:** prolonged use of **corticosteroids** (as patients with status asthmaticus) or **muscle relaxants** (as patients on prolonged mechanical ventilation which is associated with β_2-agonists).
- **Disuse atrophy.**
- **Catabolic states.**

Clinical Picture:

- Although common, these neuromuscular disorders **often go undetected because they are overshadowed** by the more prominent clinical manifestations of the inciting condition.
- Neuromuscular disorders (and muscle weakness) **are suspected in critically ill patients,** after the underlying illness begins to resolve, in the following conditions:

- Failure to wean from mechanical ventilation.
- Limb weakness on stoppage of sedation .

• Muscle weakness may be profound and **persist for weeks to years**. Occasionally, it **may be permanent**.

Investigations:

• **Electromyography.**
• **Nerve conduction studies.**

Variable degrees of neuropathy and myopathy may be detected by the above investigations.

• **Muscle biopsy** may show fiber atrophy, mitochondrial defects, myopathy, and necrosis.

a) Critical Illness Polyneuropathy:

• It is characterized by **an acute idiopathic diffuse sensory and motor axonal degeneration** (neuropathy) with **flaccid weakness** following a prolonged period of intensive care.

• Nerve conduction velocities are normal indicating no demyelination. Cerebrospinal fluid is normal unlike Guillain-Barré syndrome.

• **Recovery:** requires multidisciplinary teamwork for **rehabilitation and management of neuropathic pain. Pyridoxine** (100-150 mg/day orally) is used in treatment, but not evidence-based. **Intensive insulin therapy** (to achieve tight control of blood glucose) can reduce the incidence of critical illness polyneuropathy by 44%.

b) Critical Illness Myopathy:

• It is characterized by **diffuse weakness and depressed deep tendon reflexes.**
• There is **mild elevation of creatine kinase** in 50% of cases
• It may be associated with **renal impairment due to myoglobinuria.**
• **Recovery:** requires multidisciplinary teamwork for rehabilitation.

Channelopathies

Definition:

They are a group of inherited diseases caused by mutations in genes coding for Na^+, Cl^-, K^+, and Ca^{++} channel subunits.

Composition of Ion Channels:

Ion channels are macromolecular protein tunnels that span the cell membrane. The direction of ionic movement is governed by electrical and chemical concentration gradients.

Most ion channel proteins are composed of individual subunits or groups of subunits assembled around a central ion-selective pore. Each subunit contains 4 domains (I, II, III, and IV), which in turn, each contains 6 helical trans-membrane units (S_1-S_6). Alpha subunits appear to be the most important of all subunits.

Heritable Diseases Associated with Channelopathies:

Ion Channel Disease	Inheritance	Channel Defect	Remarks
1- Myotonia congenita (Thomson's disease)	AD	Na^+	See chapter " Neuromuscular Disorders"
2- Myotonia congenita (Becker's disease)	AR	Cl^-	
3- Para-myotonia congenita.	?	Na^+	
4- Hyperkalemic periodic paralysis	AD	Na^+	
5- Hypokalemic periodic paralysis	AD	Ca^{++}	
6- Malignant hyperthermia	AD	Ca^{++}	See chapter "Problems with Anesthesia & Intensive Care"
7- Masseter muscle rigidity	?	?	
8- Central core disease	AD	Ca^{++}	
9- Cystic fibrosis	AR	Cl^-	See chapter "Respiratory Diseases"
10- Long QT syndrome: Type I and II. Type III.	AD/AR AD/AR	K^+ Na^+	See chapter "Cardiovascular Diseases"
11- Heritable hypertension (Liddle's syndrome)	AR		
12- Familial persistent hyper-insulinemic hypoglycemia of infancy.	AR		
13- Hereditary nephrolithiasis (Dent's disease)	XL		

A = autosomal R = recessive. D = dominant XL = sex-linked

Drugs affecting Ion Channel Function:

Drug	Channel affected
1- Calcium channel blockers.	Ca^{++} channels.
2- Potassium channel blockers.	K^+ channels.
3- Anti-arrhythmic drugs (amiodarone).	K^+ channels.
4- Anti-hypertensive drugs (diazoxide).	K^+ channels.
5- Adenosine.	K^+ channels.
6- Diuretics (amiloride).	Na^+ channels.
7- Anticonvulsants (carbamazepine, phenytoin, and valproate).	Na^+ channels.
8- Class I anti-arrhythmics.	Na^+ channels.
9- Local anesthetics (lignocaine and bupivacaine).	Na^+ channels.
10- Anticonvulsants (clonazepam and phenobarbitone).	Cl^- channels.
11- Benzodiazepines.	Cl^- channels.

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PLASTIC SURGERY

28

• Maxillofacial (or craniofacial) reconstruction and orthognathic surgery • Cleft lip and palate • Mandibular hypoplasia • Hypertelorism • Limb surgery • Breast reduction	• Breast augmentation • Correction of prominent ears • Facelift (rhytidectomy) • Free flap surgery • Liposuction • Burn

Plastic surgery includes the reconstitution of damaged or deformed tissues (congenital abnormalities or resulting from trauma, burns, or infection), removal of cutaneous tumors or cosmetic alteration of body features. Plastic surgery also includes skin grafting, free and pedicle grafts. Maxillofacial and orthognathic surgeries are sometimes included in plastic surgeries or considered as a separate entity. Microvascular limb surgeries are also considered as a part of the plastic surgeries such as limb or digit re-implantation.
Minor procedures are suitable for surgery as a day case e.g., correction of prominent ears, Dupuytren's fasciectomy, or the excision of skin lesions.

Maxillofacial (and Craniofacial) Reconstruction and Orthognathic Surgery

Maxillofacial reconstruction is indicated in:

- Fractures e.g., Le Fort fracture.
- Congenital anomalies e.g., hypertelorism and facial cleft.
- Radical cancer surgery e.g., mandibulectomy or mandibular hypoplasia.
- Cleft lip and palate.

Orthognathic surgery is indicated in:

- Dental surgeries e.g., Le Fort osteotomies and mandibular osteotomies.
- Mal-occlusion.

Anesthetic Management:

Anesthetic Problems and Considerations:

1- Airway management: pre-, intra-, and postoperative.
2- Associated injuries, in case of trauma.
3- Risk of aspiration in case of trauma.
4- Increased blood loss.
5- Oropharyngeal packs.
6- Postoperative jaw-wiring.

Preoperative Management:

1- Preoperative Assessment of the Airway:

- Preoperative assessment of the airway is important in these patients especially for jaw opening, mask fitting, neck mobility, micrognathia (a small mandible), retrognathia (receding of the lower jaw), maxillary protrusion, macroglossia (a large tongue), dental pathology, and nasal patency.
- **The degree of airway obstruction** e.g., aspirated teeth or oral bleeding should be assessed especially in maxillofacial trauma. First, ensure patency of the airway during patient resuscitation by holding the tongue, lateral head position, good suction…etc.
- X-ray, CT scan, and reconstructive CT scan are usually indicated (figure 28-1 and 28-2).

2- Preoperative Assessment of Other Injuries (in case of trauma).

For example, basilar skull fracture for rhinorrhea, intracranial, abdominal, or thoracic injuries.

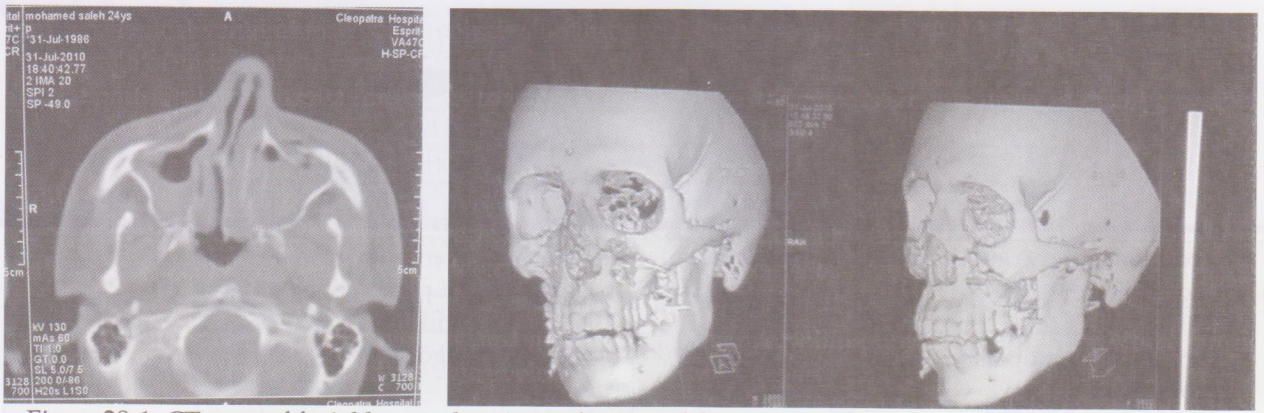


Figure28-1: CT scan of facial bones showing a depressed fracture of the anterior wall of the left maxilla and its reconstructed 3-D images

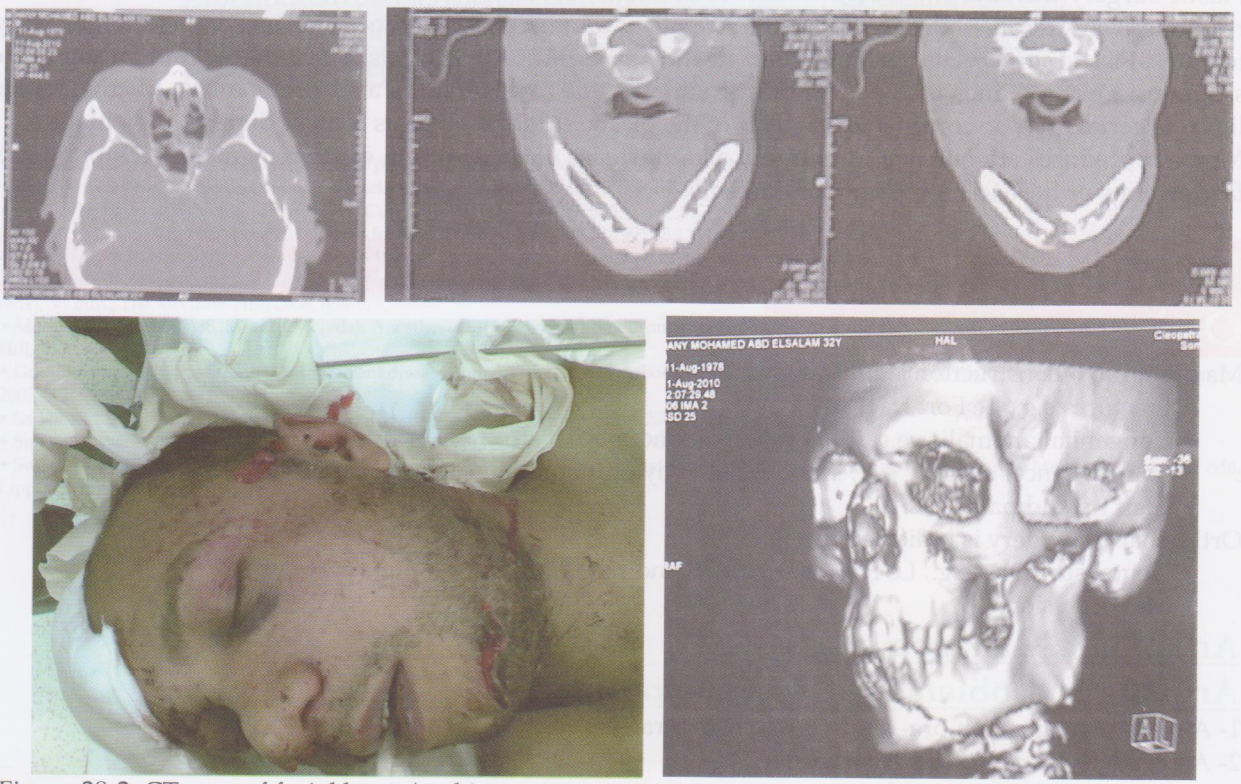


Figure 28-2: CT scan of facial bone (and its reconstructive image) showing a depressed fracture of the left temporal bone and fracture of the mandible

3- Patient Preparation:

- **ABCD resuscitation protocol** in case of trauma should be applied first.
- **I.v. access** may need extension tubing if the cannula is in the arm during surgeries in head and neck.

4- Premedication:

1- Sedatives: are avoided in case of possibility of airway obstruction.

2- Aspiration prophylaxis measures (in case of trauma) such as nasogastric suction, antacids, H_2 blockers and metoclopramide.

Intraoperative Management:

Monitoring: Besides the standard monitors, the choices of monitors depend on the patient's condition.

- A **foot should be exposed** to allow clinical monitoring e.g., color, capillary filling...etc.
- Disconnection alarm and an esophageal stethoscope (to monitor breath sounds) are important because there is a risk of tube disconnection or kinking.

Induction and Intubation:

One of the following techniques can be chosen according to the patient's condition.

a- **Awake intubation** by fiberoptic bronchoscopy in **cooperative** patients may be done.

- **Oral intubation:** It is usually preferred especially in case of face trauma.
- Nasal intubation: It may be done, but is usually contraindicated in case of face trauma.
- Even tracheostomy under local anesthesia can be done.

b- **Inhalational induction** in **uncooperative** patients may be done.

Both a- and b- are indicated in cases of suspected difficult intubation or airway obstruction. A complete range of equipment should be available.

c- **Rapid sequence induction** is indicated if there is a risk of **aspiration**.

- An endotracheal tube should be a reinforced **armored tube** and should be efficiently secured in place and to the anesthetic circuit connections.
- A posterior **oro-pharyngeal pack** is inserted after intubation and induction to prevent blood and debris from reaching the larynx. There should be a mark indicating its presence and it should be removed before extubation.

Patient Position:

As in most of head and neck surgeries, **the patient is put in a 10-15 degrees head-up** tilt to help venous drainage.

Protection of eyes and ears from pressure, trauma, blood, and debris are mandatory.

Maintenance: The anesthetic technique should allow early recovery.

Intraoperative Problems: There is an **increased risk of blood loss** in these surgeries; therefore,

- 2 large bore i.v. cannulas should be placed.
- Cross-matched blood units are prepared.
- A slight head-up position is maintained.
- Local infiltration with epinephrine is advised.
- Invasive blood pressure monitoring is usually used. Noninvasive arterial blood pressure may be unreliable because surgeons may lean against the patient's arm interfering with the blood pressure cuff reading.
- Controlled hypotensive anesthesia is sometimes used.

Extubation: Awake extubation in the lateral position is advised.

Postoperative Management:

1- Postoperative **edema of the airway** such as edema of the tongue or larynx may occur; therefore, the patient may remain intubated postoperatively.

2- If the jaws are wired and fixed in full occlusion, a pair of **wire cutters** must be kept always by the patient's **bedside** to release the jaw fixation if vomiting occurs.

Cleft Lip and Palate

Incidence:

- Isolated cleft lip represents 25% of patients with this defect.
- Isolated cleft palate represents 25% of patients with this defect.
- Cleft lip and palate represents 50% of patients with this defect.
- Cleft lip (with or without palate) is more in males while isolated cleft palate is more in females.

Types:

a- Cleft Lip: is bilateral or unilateral, complete or incomplete (figure 28-3).



Figure 28-3: Two different children; cleft lip (left) and cleft lip and palate (right)

b- Cleft Palate: (figure 28-4).

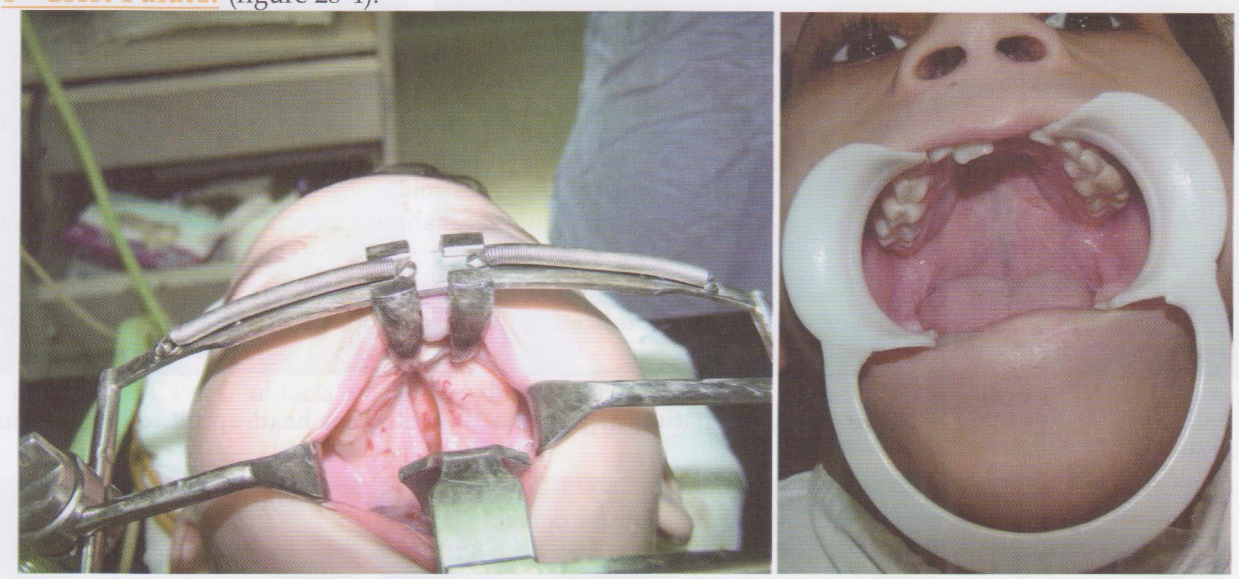
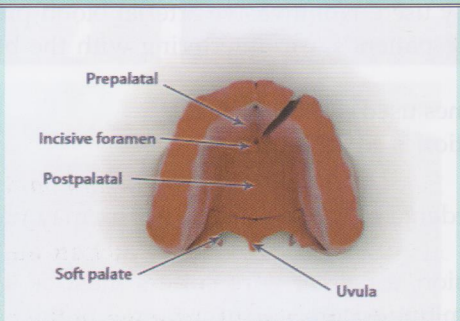
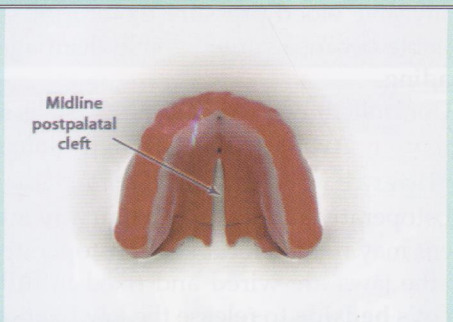


Figure 28-4: Two patients with cleft palate; the left one is complete post-palatal with a Dingman retractor in place while the right one is incomplete (sub-mucosal type) post-palatal

	Pre-Palatal Cleft	Post-Palatal Cleft
	 Figure 28-5	 Figure 28-6
Site	**Anterior** to the incisive foramen (figure 28-5).	**Posterior** to the incisive foramen (figure 28-6).
Components	Anterior palate, alveolus, lip, nostril floor and ala nasi.	Posterior palate, soft palate, and uvula.
Subtypes	Complete or incomplete.	Complete or incomplete depending on the extension through the way between the soft and hard palate to the incisive foramen.
Incidence	**Left complete pre-palatal cleft** is the 1st most common type.	**Midline cleft of all the soft palate and part of the hard palate** (without reaching the pre-palatal area) is the 2nd most common type.

N.B.: Sub-mucosal cleft is a bone defect without a mucosal defect.

Anesthetic Management:

Preoperative Management:

1. Preoperative Assessment and Management of Clinical Picture:

- **Feeding problems:** are usually present. There is **failure to thrive** (so, the body weight should be increased), and **anemia** (it should be treated preoperatively to be ≥ 10 gm %). The neonate **cannot suckle** because the cleft makes the creation of negative pressure difficult.
- **Chocking and aspiration**: may cause repeated upper respiratory tract infections and chronic middle ear infections (it can cause conductive hearing loss). Patients should be free from acute infections preoperatively i.e., white blood cell count should be < 10 000/mm^3.

Nasal separation between food and air is absent creating a non-physiological mixing chamber in the nasopharynx leading to chronic rhinorrhea that must be distinguished preoperatively from infection.

• **Speech problems** (in older children): may be present. **Hyper-nasality** (i.e., increased nasal tone) and inability to sound plosives (P, K, D, T) and sibilants (S, Sh) are common findings. There is **velo-pharyngeal incompetence** because to produce those sounds, the soft palate must touch the posterior pharyngeal wall to close the nose; otherwise, hyper-nasal speech occur.

N.B.: **Velo-pharyngeal Incompetence:**

It is diagnosed by:

- Direct vision of the soft palate while the child is pronouncing certain key words (Kah, Kah).
- Fogging of a hand mirror placed under the nose during speech.
- Cine-fluoro-graphic x-ray films.

Velo-pharyngeal incompetence may occur due to other causes such as:

- Patients with **short palates** without cleft; they need surgical lengthening of the palate by the push-back operation ± a pharyngeal flap.
- **After adenoidectomy or tonsillectomy**, because the adenoid and tonsils tend to close the naso-pharynx.

• **Psychological problems:** may occur especially as this youngster approaches school age and peer association.

2. Preoperative Assessment for Other Associated Congenital Anomalies:

Congenital anomalies are 30 times more common than in non-cleft patients, for example, congenital heart disease, Pierre Robin syndrome, Down syndrome, umbilical hernias, or limb and ear deformities.

3. Time of Surgery:

For cleft lip, the 1st week of life is the best time for surgical repair (cheilopalsty) to allow proper feeding.

For cleft palate, the 1st year of life is the best time for surgical repair (palatoplasty) to allow proper speech.

4. Premedications:

Sedatives: are usually not needed.

Intraoperative Management:

Induction and Intubation:

• According to the presence of **airway obstruction**,

- If there is **no airway obstruction** e.g., by other anomaly, **i.v. induction and intubation** are recommended.
- If there is **airway obstruction** e.g., by other anomaly, **inhalational induction and intubation** are recommended.

• If muscle relaxants are required for intubation, **assess the facial configuration** of the patient to assess if it allows effective controlled mask **ventilation** or not.

• Laryngoscopy is done with care to avoid falling into the cleft and causing trauma; so, insertion of a small piece of gauze or dental roll to fill the gap may be needed.

• **The endotracheal tube:**

- The **preformed RAE tubes** are of choice to curve away from the surgical field.
- **Non-kinkable tubes** are used to avoid occlusion by the palate retractor.
- The **tube is fixed to the lower lip** in the midline to avoid distortion of the facial anatomy unlike other pediatric cases in which the tube is fixed to the upper lip and maxilla to avoid its advancement into the bronchus due to the high mobility of the lower mandible.
- The tube is held under the tongue blade of the mouth gag. Care should be taken to avoid its advancement into the main bronchus or dislodgement from the trachea. Breath sounds should be monitored when the gag is opened. If any change occurs, the gag should be closed and the tube repositioned until the breath sounds are normal with the gag fully opened (also end-tidal CO_2 is important).

• **A Pharyngeal pack is usually inserted** to protect against food or blood aspiration.

• **An Eye cover:** is important.

• **Lidocaine** (maximal dose 5 mg/kg) with **epinephrine** (maximal dose 10 µg/kg) can be used for infiltration.

Maintenance:

O_2: air (N_2O) + Halothane or sevoflurane + a muscle relaxant + controlled mechanical ventilation.

Extubation and Recovery:

• **Awake extubation** in the lateral position is done after good suction under vision and removal of the pack.

• **Avoid the use of oral or nasal airways** as they may disrupt the surgical sutures.

• **Traction sutures** may be placed through the **middle of the tongue** and taped to the cheek. In cases of postoperative airway obstruction, the tongue should be pulled forward with the suture to open the airway. It is removed when the infant leaves the recovery room.

Postoperative Management:

It is usually in an intensive care unit for 24 hours at least.

Postoperative Complications include:

1- Hemorrhage.
2- Respiratory obstruction; so, keep patients in the semi-sitting position with the head extended to one side.
3- Hypothermia.
4- Breakdown of the sutures.
5- Scarring.
6- Infection.

Mandibular Hypoplasia

It is present in:

1. Pierre Robin Syndrome

Anesthetic Problems:

- Hypoplasia of the mandible **(micrognathia).**
- Posterior displacement of the chin **(retrognathia).**

Both cause **difficult intubation and airway management**.

- Posterior displacement of the tongue **(glosso-ptosis):** The tongue falls back causing **acute airway obstruction.**
- **Cleft palate** causing feeding problems.
- Congenital **heart** disease.

2. Treacher Collins Syndrome (it is autosomal dominant)

Anesthetic Problems:

- Hypoplasia of the mandible **(micrognathia).**
- Molar bone hypoplasia with malocclusion (anterior open bite).

Both cause **difficult intubation and airway management**.

- Notching of the lower eyelids **(Colobomas)** and anti-mongoloid slant of the eyes.
- **High arched or cleft palate** causing feeding problems.
- **Microtia** (small external ear) with possible hearing loss.
- **Macrostomia** (abnormally large mouth)
- Congenital **heart** disease especially ventricular septal defects.

3. Goldenhar Syndrome

Anesthetic Problems:

- Unilateral hypoplasia of the mandible (micrognathia).
- Associated eye, ear, and vertebral anomalies on the affected side (figure 28-7).



Figure 28-7: Pierre Robin (left), Treacher Collins (middle), and Goldenhar (right) syndromes

Hypertelorism

It is present in:

1. Crouzon's Syndrome

- Increased distance between the eyes **(hypertelorism).**
- Premature closure of cranial sutures **(craniosynostosis).**

- Shallow orbit and mid-face hypoplasia causing **marked proptosis** (figure 28-8).



Figure 28-8: A patient with Crouzon's syndrome showing obvious hypertelorism

2. Apert Syndrome

- The same anesthetic problems as these of Crouzon's disease, in addition to **syndactly** of all extremities (figure 28-9).



Figure 28-9: A patient with Apert syndrome; the upper images show slight hypertelorism and mid-face hypoplasia with slight proptosis while the lower images show **syndactly** of all extremities

3. Robinow Syndrome

Robinow syndrome is an extremely rare genetic disorder characterized by short-limbed dwarfism, abnormalities in the head, face (hypertelorism), and external genitalia, as well as vertebral segmentation (figure 28-10).



Figure 28-10: Robinow syndrome

Other Anomalies Associated with Hypertelorism:

- Cleft palate.
- Craniosynostosis (figure 28-11).
- Synostosis of the cervical spine.
- Hearing loss.



Figure 28-11: Two different cases with orbital hypertelorism

Other Cranio-Facial Anomalies

These anomalies such as facial cleft, plagiocephaly, trigonocephaly, cloverleaf syndrome, and Pfeiffer syndrome require extensive maxillofacial and craniofacial surgery, which may last many hours (figure 28-12).



Figure 28-12: Craniofacial anomalies; facial cleft and phocomelia (short upper limbs) (upper left image), plagiocephaly (upper middle image), and trigonocephaly (upper right images), Cloverleaf syndrome (lower left and middle images), and Pfeiffer syndrome (lower right image)

Anesthetic Problems of Craniofacial Surgery:

1- Difficult Tracheal Intubation Versus Elective Tracheostomy 3 days before the surgery.

- It needs proper preoperative assessment and preparation.

2- Problems due to Face Surgery

- Possibility of **tube kink** (needing an armored tube) or **tube displacement** (needing proper fixation and observation) or **disconnection** (needing an alarm).
- Possibility of **corneal abrasion** especially if with proptosis (needing eye protection).

3- Problems due to Lengthy Surgery (may last up to 18 hours).

- Intraoperative **hypothermia.**
- Intraoperative **fluid** management.
- **Pressure necrosis and nerve injury**; it needs careful positioning and padding.

4- Excessive Blood Loss:

- Elevate head up by 15-20°C.
- Invasive monitoring.
- Large venous access.
- Preoperative blood preparation.

5- Intracranial Hypertension.

6- Postoperative Mechanical Ventilation of the lungs for several days as the entire head may be wrapped in pressure dressings through which only the endotracheal tube protrudes.

Limb Surgery

It is usually limb re-implantation by microsurgical re-anastomosis of vessels and nerves (figure 28-13). The patient is young and healthy with a traumatic limb or hand, or finger amputation. These reconstructive procedures may take many hours (up to 12-24 hours).

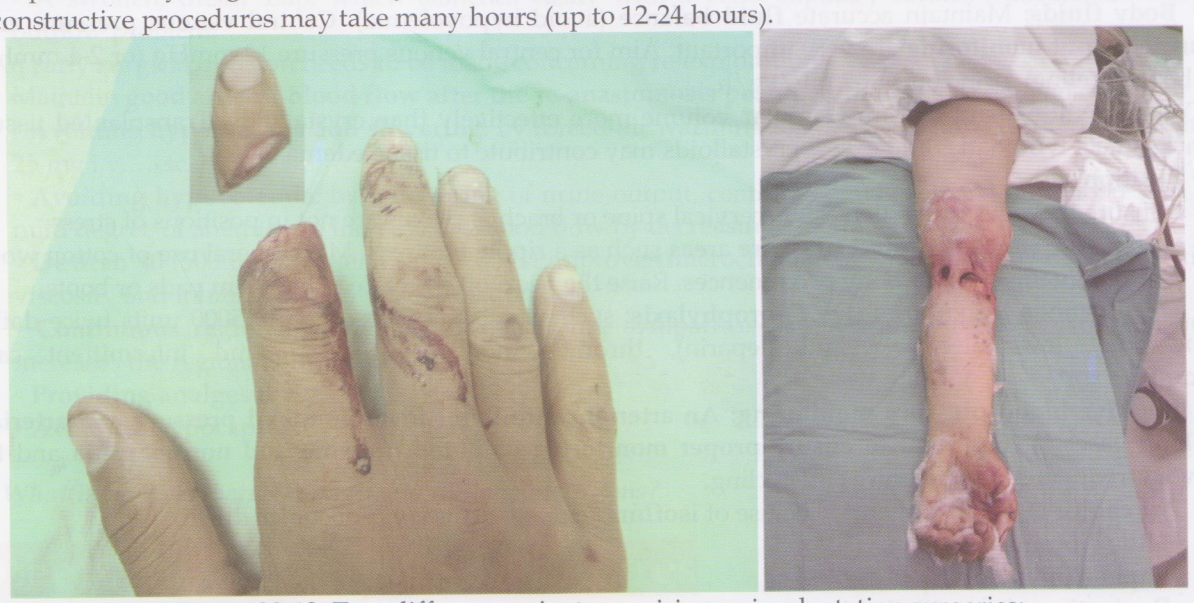


Figure 28-13: Two different patients requiring re-implantation surgeries; the left one with a trauma in the index finger while the right one below elbow

Free flap surgery should be managed as for re-implantation of severed digits or limbs.
Sometimes reconstructive limb surgeries are needed for other cases such as lower limb lymphedema (figure 28-14).

Anesthetic Problems and Considerations: (of Long Operations)

1- Regional (local) anesthesia is preferred, but there are 2 disadvantages:

- **Bier's block** is of **limited** value because the **surgeon** often requires **cuff deflation to identify the bleeding points.**
- **The duration** of some surgeries may **exceed the local anesthetic technique** duration; therefore, an epidural catheter is preferred.

2- Prolonged general anesthesia requires the following precautions:

- **Body temperature:** Maintain body **temperature** (avoid hypothermia), with monitoring core temperature (e.g., rectal, nasopharyngeal, or esophageal), using low fresh gas flows, a heat-moisture exchange (HME) filter, warmed i.v. fluids, a warm ambient theater temperature (e.g., 24 °C), a heated mattress, or external warming blankets. Take care not to overheat.



Figure 28-14: Lymphedema

• **Body fluids:** Maintain accurate **fluid balance** (avoid hypovolemia). **Central venous pressure and urine output monitoring** are very important. Aim for central venous pressure 12 mmHg (or 2-4 mmHg above baseline), urine output 2 mL/kg/h.
Colloids will expand the intravascular volume more effectively than crystalloids. Transplanted tissue lacks intact lymphatics and excess crystalloids may contribute to tissue edema.

• **Positioning:**
  ▫ Ensure that structures such as the cervical spine or brachial plexus are not in positions of stress.
  ▫ Apply measures to **protect pressure areas** such as a ripple mattress. Make liberal use of cotton wool padding (gamgee) over bony prominences. Raise the heels off the table using foam pads or boots.

• **Deep venous thrombosis (DVT) prophylaxis:** such as subcutaneous heparin 5000 units twice daily (or daily low-molecular-weight heparin), thrombo-embolism stocking, and intermittent calf compression.

• **Invasive blood pressure monitoring: An arterial cannula** for invasive **blood pressure** and **arterial blood gases is important to ensure proper monitoring of blood pressure and normocapnia** and to avoid frequent blood pressure cuff cycling.

• **The choice of volatile agents:** The use of **isoflurane or sevoflurane** is of choice due to:
  ▫ Little biotransformation.
  ▫ Rapid elimination.
  ▫ Production of vasodilation in normovolemic patients, which is beneficial to the outcome of surgery.
  ▫ **Avoid N_2O** as on prolonged exposure, it causes bone marrow depression, megaloblastic anemia, agranulocytosis, peripheral neuritis, and interference with immune response.

• **Nasogastric tube:** Consider emptying the stomach. Children are especially prone to **gastric distension** during prolonged procedures.

• **Eye care:** Lightly tape and pad the eyes for protection and for avoiding corneal abrasions from surface drying. Avoid excessive padding, since this may negate the natural protection afforded by the bony orbit. Prophylactic antibiotic ointment is unnecessary.

• **Endotracheal tube cuff pressure:** Cuff pressure will gradually increase if N_2O is used. Where possible, recheck the cuff pressure at intervals during the case. Alternatively, fill the cuff with N_2O-containing gas or saline from the start.

• **Smooth extubation** is beneficial to avoid stress-induced vasoconstriction.

3- Avoid vascular spasm in the limb by:

• **Preoperative i.v. sympathetic blockade**. This is indicated in vascular re-anastomosis surgical procedures. This can be achieved by guanethidine 15-20 mg, heparin 5000 units, and prilocaine 0.5%.

• A regional block is helpful to supplement anesthesia. The **sympathetic block and dense analgesia** produce excellent conditions for graft survival due to the vasodilation.

• Blood flow through the microvasculature must be optimal to help ensure flap survival. Blood flow is primarily influenced by changes in **perfusion pressure, caliber of vessel, and blood viscosity** (Hagen-Poiseuille formula). These factors should be controlled to help perfusion via the microvasculature. Aim for a hematocrit of 30%, which is the best figure to balance between low blood viscosity, arterial oxygen content, and tissue oxygen delivery.

• **Monitor** core (e.g., rectal, esophageal) and peripheral temperature. Aim for normal or even supra-normal core temperature and **a core-peripheral difference of <2 °C**. Widening of the core-peripheral temperature difference may herald vasoconstriction.

Potent vasodilators (e.g., sodium nitroprusside, hydralazine, and phenoxybenzamine) are unnecessary. Sufficient vasodilation can be produced by the anesthetic agent provided that the patient is warm, volume loaded, pain free, and normocarbic. **Nifedipine** (10 mg/ 8 hours i.v.) or **chlorpromazine** (1-2 mg i.v. diluted) is useful to narrow a widened core-peripheral temperature difference when all other factors have been corrected. **Papaverine** may be injected directly by the surgeon in the vessels to prevent local spasm.

4- Postoperative management:

• The patient can be transferred **to ward or intensive care/high-dependency unit** according to the patient's medical condition.

• **Continue meticulous care and observation** to detect early signs of ischemia. This is a job of a specialized nurse. A flap chart containing temperature, color, and arterial pulse (using a Doppler probe if possible) is mandatory.

▫ A pale, pulseless flap with sluggish capillary filling may indicate problems with the arterial supply.

▫ A swollen, dusky flap, which blanches easily with a brisk capillary return, indicates a venous outflow problem.

An early surgical decision needs to be made concerning re-exploration.

• Maintain **good arterial blood flow after the re-anastomosis postoperatively**. This depends on:

▫ Avoiding **hypothermia and shivering:** by forced-air warming blankets, i.v fluid warmers, pethidine 25 mg i.v....etc.

▫ **Avoiding hypovolemia:** by monitoring of urine output, central venous pressure, and blood loss. A mild degree of anemia can increase the blood flow by decreasing blood viscosity.

▫ **Dextran 40** (500 mL i.v. daily for 2-3 days) improves microcirculatory blood flow by decreasing the viscosity and inhibiting the platelet function.

▫ **Continuous regional nerve blocks** may cause sympathectomy resulting in vasodilation, which increases the regional blood flow.

▫ **Providing analgesia**

▫ **Avoiding hypocapnia.**

Q: What is the anesthetic management in long operations?

Other Plastic Surgical Procedures

1- Breast Reduction

Bilateral breast reduction is usually indicated not only for cosmetic (aesthetic) reasons but also may be indicated in patients suffering from severe neck and back pain. There may be also symptoms of emotional disturbances (figure 28-xxxxxx).

A mastopexy is a surgical procedure for correcting breast ptosis when breast volume is adequate.

Anesthetic Problems and Considerations:

• Patients should receive **balanced general anesthesia**. **Mechanical ventilation** may be preferable since the surgeon often puts pressure on the chest wall during surgery. Mechanical ventilation will maintain satisfactory chest expansion with good aeration, control of $PaCO_2$ and help minimize blood loss. A laryngeal mask airway is usually satisfactory for mechanical ventilation except for obese patients in whom intubation is mandatory.

• Loosen and remove the theater gown prior to induction. Place **ECG electrodes on the patient's back**. Place the patient on incontinence pads to absorb blood lost.

• Positioning:

▫ Ensure that **the chest and arms are symmetrical** during the procedure.

- Confirm that the **cannulas** are firmly positioned and their plastic caps covered with gamgee (cotton wool padding) if the hands are to be positioned behind the buttocks. Local pressure damage to skin may otherwise ensue. Drip extension sets are usually needed.

• **Blood loss** is usually **not severe** except if very large breast volume is present. Infiltration with dilute adrenaline-containing local anesthetic helps reduce blood loss. Fewer than 5% of patients usually require transfusion. Mild falls in hemoglobin are well tolerated in this predominantly young patient group.

• **Postoperative complications** include:

- Hematoma formation that is an early complication.
- Occasionally, nipple perfusion may be compromised and require decompression of the pedicle where return to theater may be indicated. Sometimes, ischemia and loss of the nipple may occur.
- Wound infection, dehiscence, and fat necrosis may also occur.

2- Breast Augmentation

Conventional augmentation involves creation of a subcutaneous pocket for a silicone implant via an infra-mammary incision.

Modern techniques involve initial pocket formation by the insertion of an inflatable capsule mounted on an introducer via a small incision in the anterior axillary line. This is then removed and the implant inserted. There is early recovery and there is less postoperative discomfort.

Breast augmentation is usually indicated not only for cosmetic (aesthetic) reasons, but also may be indicated in:

- Reconstruction following mastectomy.
- Correction of breast symmetry. Minor asymmetry is common. In its most severe form, there may be unilateral absence of breast tissue and pectoralis major muscle (Poland syndrome).

Anesthetic Problems and Considerations:

• **Positioning**: is the same as breast reduction (see above).

• Breast augmentation appears to cause **more postoperative discomfort** than breast reduction especially with large implants due to tissue stretching and postoperative pain.

• **Postoperative complications** include:

- Hematoma formation that may require early return to theater.
- Infection, capsule formation, prosthesis rupture, or skin erosion that may occur.

• Breast reconstruction following mastectomy is common. Options include insertion of a breast implant, reconstruction with a pedicled myocutaneous flap (e.g., latissimus dorsi or transverse rectus abdominis muscle "TRAM"), or a free flap repair (usually TRAM).

3- Correction of Prominent Ears

Anesthetic Problems and Considerations:

• Day case anesthetic technique is usually indicated.

• Postoperative nausea and vomiting are common.

• The surgeon uses extensive local anesthetic/adrenaline infiltration to aid hemostasis.

• Dressings should be firm without being excessively tight. Allow time for extensive bandage at the end of the operation especially if an endotracheal tube is used; otherwise, coughing can occur when the head is manipulated for bandage application. A laryngeal mask airway is a good alternative (figure 28-15).

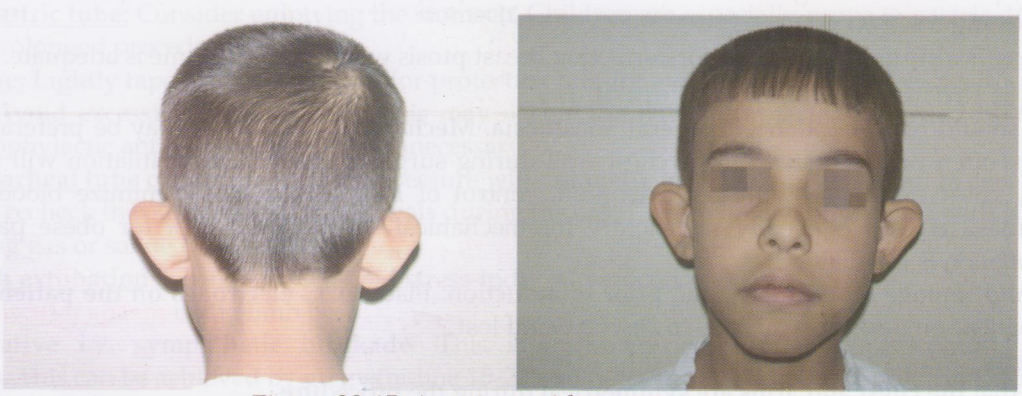


Figure 28-15: A patient with prominent ears

4- Facelift (Rhytidectomy)

Incisions are placed in concealed areas (e.g., preauricular, extending up to the temporal region within the hair). The skin is mobilized by subcutaneous undermining and wrinkles/skin folds are improved by traction. Redundant skin is excised. Surgery is adapted to suit the needs of the patient and may include forehead lift, upper and lower blepharoplasty, and removal of subcutaneous/submandibular fat.
The observed benefits from facelift procedure may only last 3-5 years. Repeated operations are common. Some patients may undergo several facelifts during their lifetime.

Anesthetic Problems and Considerations:

- Most patients are aged 45-65 years. Patients are usually fit and well.
- Non-steroidal anti-inflammatory drugs should be discontinued for at least 2 weeks prior to surgery.
- Its usually performed under local infiltration alone but sometimes, general anesthesia may be required.
- A moderate hypotensive technique (70-80 systolic) and 30° head up tilt will help minimize blood loss and improve surgical conditions.
- A smooth emergence is important to avoid bleeding beneath delicate suture lines. Bleeding and hematoma formation may require an early return to theater.

5- Flap Surgery

Flaps (e.g., free flaps and pedicled flaps) are most commonly used to provide tissue cover following trauma, bed pressure sore, or resection for malignancy. It is one of the long procedures. Free flaps are microvascular procedures (figure 28-16).

Anesthetic Problems and Considerations:

- As it is a microvascular procedure, the aim of anesthesia is to produce **a hyperdynamic circulation with high cardiac output, adequate vasodilation, and wide pulse pressure**. The elderly or patients with limited cardiopulmonary reserve may not be suitable for surgery.
- **Precautions of long operations** should be considered (see above).



Figure 28-16: The upper images show a patient with epithelioma of the face. A large defect is present after its removal, which is covered by a pedicled flap. The lower image shows another patient with a bed sore

6- Skin graft

These surgeries are simple procedures, which may be needed to cover skin loss in many patients such as posttraumatic and postburn patients and patients with xeroderma pigmentosum (figure28-17).



Figure 28-17: Two different patients with xeroderma pigmentosum; these patients usually have difficult intubation due to contracted mouth opening and destructed nose

7- Liposuction

It includes vacuum aspiration of subcutaneous fat via a small skin incision and a specialized blunt-ended cannula. Fat is infiltrated with dilute local anesthetic with adrenaline. Back and froth movement of the cannula disrupts fatty tissue, which is then aspirated either by suction apparatus or syringe. Injection of fluid helps fat breakdown and aids aspiration.

This procedure may be indicated in:

- Lipoma removal.
- Gynecomastia.
- Reducing the bulk of transplanted flaps to make them more closely contour the surrounding skin.
- Cosmetic removal of subcutaneous fat (liposculpture) in the abdominal wall, thighs, buttocks, and arms.

Anesthetic Problems and Considerations:

- There are several recipes for **subcutaneous infiltration solutions**:
  - **Superwet technique:** 1000 mL warmed Hartmann's containing 50 mL 1% lidocaine (lignocaine) and 1 mL 1: 1000 adrenaline as popular. 1 mL infiltrate per 1 mL aspirate is commonly used.
  - **Tumescent technique:** A large volume of local anesthetic/adrenaline infiltrate is used to produce tissue turgor. 3 mL infiltrate per 1 mL aspirate are often used. This technique is used as an outpatient technique and can be performed alone without additional anesthesia or sedation, but it may provide unsatisfactory anesthesia when used alone. Additional sedation or general anesthesia may be necessary. There is a little evidence that this technique is superior to the superwet technique and may produce more complications.
- **Dose safety limits for large-volume local anesthetic infiltration** are controversial. Doses significantly higher than the conventional lidocaine (lignocaine) toxic dose (4.5 mg/kg without adrenaline and 7 mg/kg with adrenaline) are often used e.g., 30-70 mg/kg. This may be possible due to:
  - the adrenaline producing slower drug absorption,
  - the poor vascularity of fat, and
  - the aspiration of much of the infused solution before the drug has been absorbed.
- **Blood loss** depends on the volume of local anesthetic/adrenaline infiltrate used. Loss is approximately 1% of the volume of the aspirate for the tumescent technique. Blood loss may reach 40% without subcutaneous infiltration.
- Extensive liposuction **physiologically resembles a burn injury** and large fluid shifts result. Commence i.v. infusion for aspirates >1500 mL. Replace aspirate 1:1 with i.v. crystalloid.
- **Postoperative care** includes the following:
  - Pressure dressing is usually applied.
  - Monitor urine output.
  - Encourage oral fluids.
  - Check hematocrit following extensive liposuction (> 2500 mL aspirate).
  - Bruising can be considerable.
  - Use non-steroidal anti-inflammatory drugs and simple analgesics for pain relief.
- Mortality and morbidity are related to high aspiration volume and high lidocaine dosage where deaths have occurred from pulmonary edema and lidocaine (lignocaine) toxicity.

Burns

Functions of the Skin

It is the largest organ in the body. It has the following functions:

- Protection from micro-organism invasion.
- Thermal regulation.
- Fluid and electrolyte homeostasis.
- Sensation (touch, temperature, and pain).
- Vitamin D metabolism.

Classification of Burns

a) According to the Surface Area (Rule of Nine):

It expresses the extent of the burn injury as a percentage of the total body surface area (TBSA) displaying either 2nd or 3rd degree burns (figure 28-18).

- Since the area of one surface of the patient's hand (palm and digits) represents 1% of that person's total body surface, one can use that relationship in estimating the extent of irregularity disturbed burns.
- In children under age 10, this rule should be modified because the head and neck are proportionately larger than in adults, so age-adjusted nomograms **(e.g., tables of Lund and Browder)** can be used. The Lund and Browder table (figure 28-19) shows the differences in body surface area percentages in children in relation to adults. The surface areas of the head and lower extremities change significantly with age. The younger the age, the higher percentage of the head and neck.

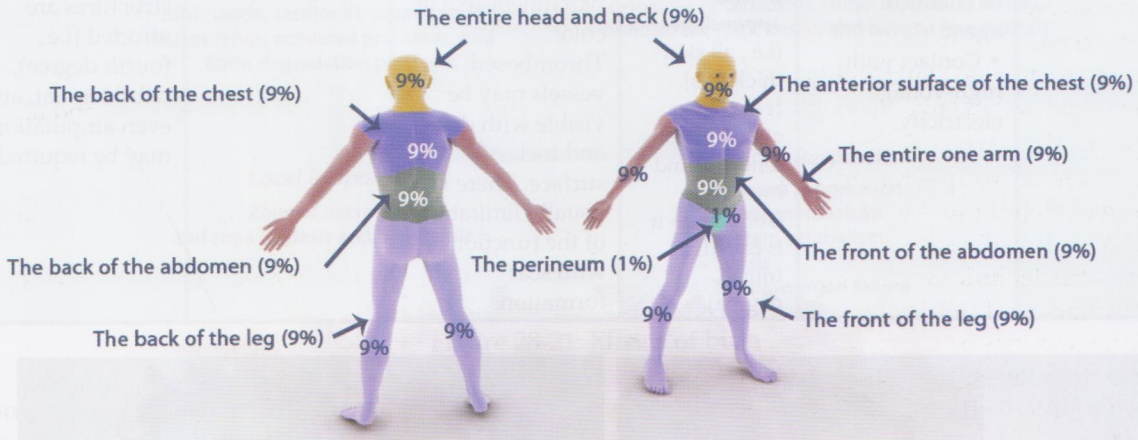
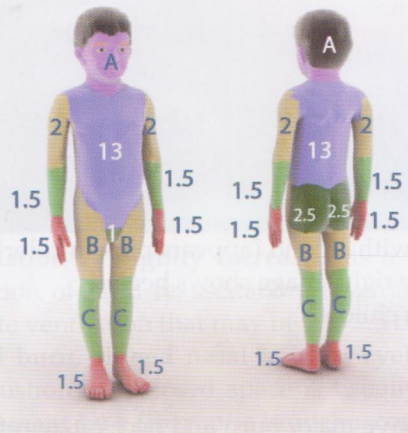


Figure 28-18: Rule of nine in adults



Body part	0 year	1 year	5 years	10 years	15 years
A = 1/2 of the head	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2
B = 1/2 of one thigh	2 3/4	2 1/4	2	4 1/4	4 1/2
C = 1/2 of one leg	2 1/2	2 1/2	2 3/4	3	3 1/4

Figure 28-19: Body surface area in a child with tables of Lund and Browder

b) According to the Depth:

Degrees of burn	Cause	Pathology	Appearance	Pain	Treatment
First Degree (Superficial)	• Exposure to sunlight. • Very brief exposure to hot liquid, flash, flame, or chemical agent.	It affects the **epidermis** only.	It appears red in color with dry surface with very small blisters.	Painful	It heals spontaneously.
Second Degree (Partial Thickness)	• Limited exposure to hot liquids, flash, flame, or chemical agent.	It affects the **epidermis** and **dermis.**	It appears pink or mottled red in color with bullae, blisters, moist or weeping surface.	Very painful	It can spontaneously heal by the epithelium around hair follicles especially in superficial dermal burn, but it requires excision and grafting for rapid return of function.
Third Degree (Full Thickness) Figure 28-20	• Prolonged exposure to flame, hot object, or chemical agent. • Contact with high-voltage electricity.	It affects the **epidermis, dermis**, and **dermal appendages** (i.e., all skin thickness). It may also affect bones, tendons, and muscles (sometimes it is called **fourth degree**).	It appears pearly white, charred, translucent, or parchment-like in color. Thrombosed vessels may be visible with dry and inelastic surface. There is usually limitation of the function with scar formation.	Not painful	It needs a skin graft for healing. When very deep structures are affected (i.e., fourth degree), debridement, and even amputation may be required.



Figure 28-20: Two burned patients; the left image shows a patient with second (appears pink in color) and third (appears pearly white in color) degree burns. The right image shows healed third-degree burn in the back of a child

Major Burns (according to the American Burn Association).

The following burn criteria are designed to identify patients who have major burn and necessitate referral to a specialized burn center:

- Partial-thickness burns greater than 10% total body surface area (TBSA).
- Third-degree (full-thickness) burns in any age group.
- Burns that involve the face, hands, feet, genitalia, perineum, or major joints.

- Electrical burns, including lightning injury.
- Chemical burns.
- Inhalational injury.
- Burn injury in patients with preexisting medical disorders that could complicate management, prolong recovery, or affect mortality.
- Any patients with burns and concomitant trauma (such as fractures) in which the burn injury poses the greatest risk of morbidity or mortality. In such cases, if the trauma poses the greater immediate risk, the patient may be initially stabilized in a trauma center before being transferred to a burn unit. Physician judgment will be necessary in such situations and should be in concert with the regional medical control plan and triage protocols.
- Burned children in hospitals without qualified personnel or equipment for the care of children.
- Burn injury in patients who will require special social, emotional, or long-term rehabilitative intervention.

Effects of Burn

Burn has local minor and major systemic effects (figure 28-21).

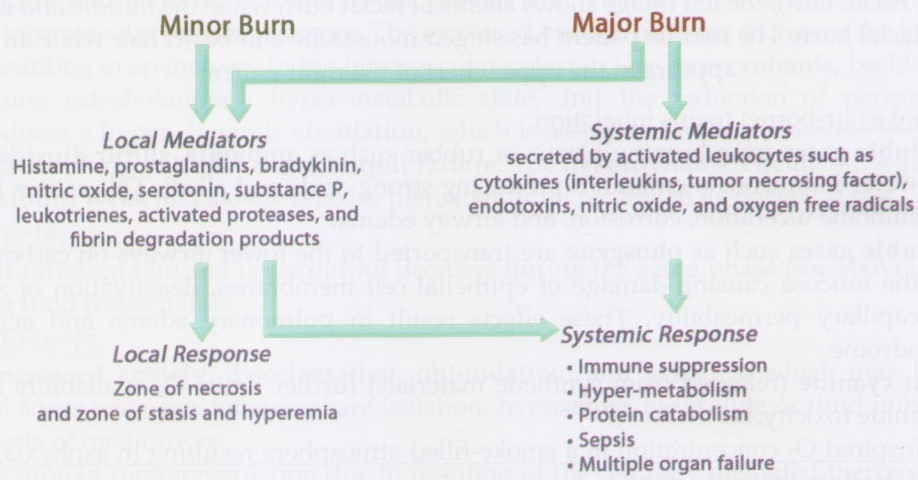


Figure 28-21: Effects of burn

Zone of necrosis: It is the burned area due to the effect of thermal injury. It is subjected to protein coagulation and cell death.

Zone of stasis and hyperemia: It is the area that surrounds the zone of necrosis, in which variable and incomplete or complete full- or partial-thickness dermal necrosis occurs. It is characterized by decreased microvascular blood flow, which may be restored to normal with successful resuscitation or converted to necrosis following inadequate perfusion, desiccation, or infection.

Systemic Effects of Burn

These effects are proportional to the size of the burn.

1) Pulmonary Effects:

1- Inhalational Injuries:

- During the **first 24 hours postburn,** usually no signs or symptoms occur (i.e., **clear or lucid interval**), sometimes, immediately postburn, even in the absence of associated smoke inhalation. **Minute ventilation** is **slightly increased** as a result of anxiety- and pain-induced hyperventilation. With the initiation of fluid resuscitation, respiratory rate and tidal volume increase progressively, resulting in a minute ventilation that may be 2 to 2.5 times normal.

Facial burn, singed nasal hair, or eyebrow, soot in the sputum or in the oropharynx, or a history of combustion in a closed space is usually suggestive of inhalational injuries, which need further **airway assessment by a fiberoptic bronchoscopy** (figure 28-22).

After the first 12-24 hours postburn, stridor, hoarseness, and **respiratory distress** may occur.

- Severe inhalational injuries produce **hypoxemia** due to one of the following mechanisms:
  - Direct thermal injury to the airway: It causes mucosal and ciliary damage resulting in airway edema and then airway obstruction (this needs early intubation even if only suspicious).



Figure 28-22: Facial burn; the left image shows chemical facial burn while the middle and right images show thermal facial burn. The middle patient has singed moustache and beard hair while an escharotomy appears in the upper chest of the right patient

- Effect of smoke (air-borne) toxins inhalation:
  - **Water-soluble gases** from burning plastic or rubber such as **ammonia, sulfur dioxide, and chlorine** react with water in mucous membranes producing strong acids and alkali. This causes bronchospasm, mucous membrane ulceration, corrosion, and airway edema.
  - **Lipid-soluble gases** such as **phosgene** are transported to the lower airways on carbon particles that adhere to the mucosa causing damage of epithelial cell membranes, deactivation of surfactant, and increased capillary permeability. These effects result in pulmonary edema and acute respiratory distress syndrome.
  - **Hydrogen cyanide** (released from synthetic materials) further limits O_2 availability and utilization causing cyanide toxicity.
- Decreased inspired O_2 concentration in a smoke-filled atmosphere resulting in asphyxia, which is the main cause of death in the acute stage.

2- Carbon Monoxide Poisoning: It causes hypoxemia.

- Carbon monoxide has a greater affinity (200 times more) for Hb than O_2, so it displaces O_2 from its Hb binding sites.
- It shifts the O_2-Hb dissociation curve to the left interfering with the unloading of O_2 at tissues.

Therefore, O_2 administration is important as the half-life of carbon monoxide can be decreased from 4 hours to 45 minutes with 100% O_2 (hyperbaric O_2 can be used in the treatment).

3- Circumferential Burns of the Thorax:

The unyielding eschar and underlying edema may decrease chest wall compliance, which increases the peak airway pressure resulting in hypoxemia i.e., a restrictive lung disease. This requires escharotomy incisions to relieve the restrictive ventilating defect.

4- During the Healing Phase of Burns:

There is increased metabolism i.e., **a hyper-metabolic state,** which increases O_2 consumption and CO_2 production. This can continue for weeks or months until healing occurs.

Q: What are the causes of hypoxemia in a burned patient?

5- Overzealous initial fluid resuscitation:

It may result in **florid pulmonary edema** as the edema fluid is resorbed during the 3rd to 5th postburn days. Consequently, the smallest volume of resuscitation fluid that maintains adequate organ perfusion should be administered to avoid secondary pulmonary complications.

2) Cardiovascular Effects (Fluid Imbalance):

1- Acute Phase (during the first 24-36 hours):

There is a large amount of **protein-rich fluid lost** from the burned wound site (due to direct thermal destruction of the capillary membrane) and from the microvascular circulation throughout the body into the interstitial fluid. This decreases **the blood volume producing burn shock** with:

- **Hemoconcentration**.

- **Increased antidiuretic hormone secretion**. The glomerular filtration rate and urine output decrease or even stop.
- **Edema all over the body** including **pulmonary edema.**
- **Decreased cardiac output** (up to 50%) due to:
  - Decreased blood volume (i.e., decreased preload).
  - Increased circulating catecholamines resulting in vasoconstriction and increased peripheral vascular resistance (i.e., increased afterload).
  - Secretion of a myocardial depressant protein, which decreases the contractility.

Decreased cardiac output decreases tissue perfusion, which further decreases the urine output. Delayed or inadequate fluid resuscitation may cause inadequate renal perfusion and lead to acute tubular necrosis and renal failure.

Decreased cardiac output decreases also hepatic functions. Serum albumin is decreased and the detoxifying effect of the liver is decreased resulting in increased free drugs as benzodiazepines and phenytoin. Serum α_1 acid glycoprotein is increased during the acute phase resulting in an increase in the binding of basic drugs e.g., muscle relaxants, lidocaine and propranolol.

2- Subacute Phase (after the first 24-36 hours):

Capillary integrity returns to normal within this period, which allows **colloids to remain intravascular,** increasing the intravascular oncotic pressure. The increased oncotic pressure increases the interstitial fluid reabsorption resulting in an increase in the intravascular volume. This **hypervolemia**, besides the increase in the circulating catecholamines, hyper-metabolic state, and the reduction of peripheral vascular resistance, produces a **hyper-dynamic circulation**, which is associated with an increase in cardiac output to supra-normal levels up to **high cardiac output failure**. The hyperdynamic circulation **reaches a peak in the second postburn week** and slowly recedes thereafter, until returns to its normal status.

3) Renal Effects:

The glomerular filtration rate and urine output decrease during the acute phase (see above). They usually increase during fluid resuscitation.

4) Nervous Effects:

- There are **increased anxiety, disorientation, obtundation, and seizures**, which may be due to the neuro-humoral stress response, intensive care isolation, hypoxemia, electrolyte or fluid imbalance, sepsis, or the toxic effects of medications.
- There is alteration of thermoregulation due to resetting of the centrally mediated thermostat; therefore, normothermia for a burned patient is about 38.5°C.

5) Electrolyte Imbalance and Drug Toxicity:

1- Hyperkalemia: occurs especially during the acute resuscitation phase due to:

- Tissue destruction.
- Hemolysis of red blood cells; anemia occurs late in recovery.
- Acidosis caused by infection.

Then **hypokalemia** may occur due to renal wasting and gastric loss.

2- Hemoconcentration (and Relative Hypernatremia): may occur due to:

- Increased aldosterone release induced by hypovolemia, which increases Na^+ reabsorption.
- Increased antidiuretic hormone release by hypovolemia, which decreases the urine output.

3- Topical Antibiotics:

For example:
- Mafenide acetate: It inhibits carbonic anhydrase enzyme resulting in hyperchloremic acidosis.
- Silver nitrate: It decreases serum Na^+, Cl^-, and K^+ and produces met-hemoglobinemia.

6) Infection and Septic Shock:

It is the major cause of morbidity and mortality in burnt patients who survive the initial insult because:

- Burned skin and eschar are a perfect culture medium.
- Loss of skin provides an easy route of entry of microorganisms into the body.
- The immune system is altered because there is alteration in the phagocytic and chemotactic properties of leukocytes.

Therefore,
- **Strict antiseptic precautions** must be applied in handling these patients to decrease the risk of cross contamination between patients.
- Quantitative **wound biopsies** are obtained to do culture and sensitivity.
- **Change catheters (urinary and intravenous),** which are cultured routinely every 3 days.

7) Hematological Effects:

Infection and burns cause:

- Subacute activation of the coagulation cascade resulting in consumption of circulating procoagulants, which produces various degrees of **coagulopathy up to disseminated intravascular coagulopathy (DIC).**
- **Decreased platelet** number and function.
- **Decreased red blood cell** survival; so, a peripheral blood smear shows many fragmented and deformed red blood cells.

8) Gastrointestinal and Hepatic Effects:

- **Ileus** occurs due to the combined effects of hypovolemia and neuro-humoral changes. Nasogastric tube for gastric decompression is usually required. Following resuscitation, normal gastrointestinal motility commonly returns by the 3rd to 5th postburn day.
- **Stress (Curling's) ulcer** occurs in 86% of cases especially a duodenal ulcer; therefore, **prophylactic antacids and H_2 blockers** are used.
- **Intestinal bacterial translocation** may occur resulting in a septic shock.
- Hepatic dysfunction occurs with elevated liver enzymes which return to normal with effective resuscitation.

9) Endocrine Effects and Hyper-metabolic Status:

- **Level:** Immediately following burn injury, during the period of hypovolemia, the metabolic rate decreases; however, as resuscitation progresses, a **catabolic or hyper-metabolic hormonal pattern** emerges. Extensive thermal injury may cause hyper-metabolic status with an increase in metabolic rates to a level **1.5-2 times normal**, far exceeding the hyper-metabolism observed in other critically ill patients. The hyper-metabolic response is linearly related to the extent of burn.
- **Cause:** The hyper-metabolic response to burn injury is partially driven by:
  - **the neuro-humoral response** produced by the hypothalamic-pituitary axis secreting **antidiuretic hormone (ADH), adrenocortico-tropic hormone (ACTH), and β-endorphins** whereas insulin and triiodothyroxine levels are decreased with **relative peripheral insulin resistance** and a **markedly negative nitrogen balance** and
  - **the autonomic nervous system,** which increases level of **catecholamines, cortisol, and glucagon.**
- **Clinical picture:** Hyper-metabolic status is manifested by increased O_2 consumption and CO_2 production, a hyper-dynamic circulation, increased core temperature, wasting of muscles and decreased lean body mass, and increased urinary nitrogen excretion.
- As the burn wounds heal or are closed by autografting, the catabolic hormone response dissipates, an anabolic state is eventually attained, and restoration of lean body mass ensues.

10) Other Effects of Electrical Burns (and Lightning Injury):

The burn occurs from the conversion of high-voltage electrical energy to thermal energy leading to:

- **Skin burns** at the site of entrance and exit.
- **Extremities** are **more vulnerable,** due to the decreased volume for diffusion of the current i.e., the current flow is concentrated through a small area (in contrast to large abdominal viscera, which are often spared, due to their large volume, which permits dissipation of the thermal insult) (figure 28-23).



Figure 28-23: Electrical burn

The current flow per unit area is known as **current density** and the greater the current density, the greater the heating effect.

- Damage of vascular endothelium resulting in **delayed thrombi** formation.
- **Muscle damage** causing release of myoglobin into the blood (**myoglobinemia**), which in turn causes **acute renal failure**. It needs aggressive volume expansion and diuresis especially mannitol.
- **Heart damage** resulting in:
  - Increased serum creatine phosphokinase (CPK-MB) isoenzyme (i.e., myocardial infarction).
  - Arrhythmias such as ventricular fibrillation.
  - Congestive heart failure.

Common Causes of Death:

- Smoke inhalation with subsequent asphyxia and adult respiratory distress syndrome.
- Irreversible burn shock (hypovolemic shock).
- Septic shock.
- Myocardial infarction (in patients > 45 years).

Management of a Burned Patient

Pre-hospital Treatment:

1- Removal of the Source of Trauma:

- **The primary concern** at the accident scene is **to stop the burning process**. Burning and smoldering clothing should be extinguished.
- Patients with **electrical injury** should be **separated from points of electric contact**, taking all necessary care to avoid injuring oneself.
- If the burn was caused by **a chemical agent**, all contaminated clothing should be removed and **copious water lavage** initiated.

2- Application of Cold Therapy:

- After patient's initial resuscitation (see later), **the application of ice or cold water soaks** will relieve pain in areas of second-degree-burn and even may decrease the depth of thermal injury **if it is applied within 10 minutes**. Care must be taken to avoid causing hypothermia. Cold therapy should only be applied for patients with burns of less than 10% of the body surface area and only for the time required to produce analgesia.

3- Covering of the Patient:

- After patient's initial resuscitation, and removal of cold therapy, the patient should be **covered with a clean sheet and blanket** to conserve body heat and minimize contamination of the burn wounds during transport to the hospital.

Resuscitation of a Burned Patient:

ABC Protocol should be first applied as follows:

1) Airway Management:

Maintaining a patent airway can be performed by bronchial suction and removal of debris. Even intubation may be necessary.

2) Breathing Management:

Adequate ventilation is maintained by mechanical ventilation with humidification of 100 % inspired O_2.

3) Circulation Management:

- Fluid resuscitation should be **started as soon as possible** following thermal injury to ensure vital organ perfusion and function.
- The order of preference for **site of i.v. cannulation** is a peripheral vein **underlying unburned skin**, a peripheral vein **underlying burned skin**, and lastly, a **central vein** to decrease the possibility of infection.
- Generally, burns involving **more than 25% of the body surface area require i.v. fluid** resuscitation because ileus precludes oral resuscitation. Patients with **smaller burns** in whom ileus does not develop should have liberal access to **electrolyte-containing fluids such as fruit juices or milk**, but excessive intake of electrolyte-free water should be avoided to prevent hyponatremia.
- There are many formulas postulated to guide fluid resuscitation in burned patients. Since these formulas are based on body weight and the percentage of total body surface area burned (TBSB), **the patient should be weighted** and **the depth and extent of burn estimated**. Only the second- and third-degree burns are considered because first-degree burns do not cause significant edema formation or

metabolic alteration and are not considered in the calculation of burn size for estimation of resuscitation requirement.

- These **resuscitation formulas** serve **only to guide** the initiation of fluid therapy. The actual amount of resuscitation fluid is tailored to **each patient's physiological responses**, with frequent reassessment and adjustment of infusion rates as needed to preserve vital organ perfusion.
- Certain subgroups of patients require a significantly **greater resuscitation volume than that estimated by the formulas** such as **delay in starting fluid resuscitation**, **inhalational injury**, **ethanol toxicity**, and **high-voltage electrical injuries.**
- In any of the following formulas, **blood transfusion is given to maintain Hb> 10 g/dL.**
- **Rate of fluid infusion** in most formulas is as follows:
  - ½ the amount is given in the first 8 hours,
  - ¼ the amount is given in the second 8 hours, and
  - ¼ the amount is given in the third 8 hours.
- The urine output should be maintained **at a rate > 0.5-1 mL/kg/h** to avoid developing renal failure; therefore, an **indwelling urethral catheter** should be inserted in all patients requiring i.v. fluid therapy, and the urinary output should be measured and recorded hourly.

Formulas found to be effective clinically include:

Formula	First 24 hours postburn	Second 24 hours postburn
1- Parkland (most common in USA). Sometimes called **Baxter** formula	**Lactated ringer's** **4 mL/kg/% burned area** of 2nd and 3rd degree burns only. No colloids are given in the first day, as they will be extravasated into the interstitial tissues via the damaged capillary walls.	• **Colloids: 20-60% of calculated plasma volume** is given as **colloids** (which are plasma equivalent) such as human albumin 5% in 0.9% NaCl solution or fresh frozen plasma. • **5% glucose in water (D_5W)** is given as necessary (about 2000 mL/24 hours) to maintain urine output and serum Na^+ concentration of 140 mmol/L.
2- Modified Brooke	**Lactated ringer's** 2 mL/kg/% burn in adults, 3 mL/kg/% burn in children.	• **Colloids**: are given according to the % of burned area as follows: ▫ **0.3 mL/kg/% of the burned area is given when the burned area is 30-50%.** ▫ **0.4 mL/kg/% of the burned area is given when the burned area is 50-70%.** ▫ **0.5 mL/kg/% of the burned area is given when the burned area is > 70 %.** • **D_5W** as Parkland formula.
3- Consensus (by the American Burn Association)	**Lactated ringer's** 2-4 mL/kg/% burn.	**Colloids and D_5W**: as **modified Brooke** formula.
4- Evans	**Normal saline** 1 mL/kg/% burn.	• **Colloids** 1 mL/kg/% burn. • **D_5W** as Parkland formula.
5- Mount Vernon (albumin-based). Sometimes called **Muir and Barclay** formula (most common in UK)	It is used in cases of > 15% burn in adults or > 10% burn in children. Type of fluid: 50% as **crystalloids** + 50% **colloid** (human albumin). The amount in mL is calculated as follows: **Body weight (in kg) × % of the burn** This amount is given in each of the following **six periods**, from the time of burning: 0-4 hours, 4-8 hours, 8-12 hours, 12-18 hours, 18-24 hours, and 24-36 hours.	

4) After Initial Resuscitation:

- The burned patient is **monitored** closely **for several days** especially for cardiovascular, respiratory, thermoregulatory, and central nervous systems on a flowsheet.
- History and examination should be taken to **search for preexisting disease, and associated trauma.**
- **Control of infection** is continued by:
  - systemic antibiotics and
  - topical antibiotics e.g., silver sulfadiazine; it has no effect on electrolytes, but on prolonged use, neutropenia and development of resistant organisms may occur.

The side effects of silver nitrate and mafenide acetate are discussed above.

- **The tetanus immunization status** of the patient should be determined in the emergency department.

- The burn patient who has been immunized against tetanus previously should be given a booster dose of tetanus toxoid if the last dose has been administered more than 5 years previously.
- The burn patient with no history of active immunization should receive tetanus immunoglobulin in addition to an initial dose of tetanus toxoid.

5) Escharotomy, Fasciotomy, and Debridement:

• **Escharotomy** is making incision of dead eschar (the area with a full thickness burn). Edema formation beneath the inelastic eschar of circumferential full-thickness burns of the extremities may impair the circulation to the distal and underlying tissues. To prevent secondary ischemic necrosis of those tissues, an escharotomy may be necessary to reduce the elevated tissue pressure.
The escharotomy procedure may be performed in the intensive care unit without the use of general or local anesthesia since only insensate full-thickness burn incised (figure 28-24).

• **Debridement (excision) of necrotic tissue** is often begun within the first few days, as **early grafting** is beneficial because this allows removal of the bacterial load quickly and decreases septic complications. Coverage is obtained using either split-skin grafts from the patient's own unaffected skin, donor skin grafts, or even experimental skin. Blood loss may be rapid and massive e.g., 100 mL/1 % of body surface grafted. The exact time for this operation varies from center to center as follows:

- Some centers prefer early excision i.e., in the first 24 hours of the burn, but its disadvantage is that the patient undergoes a major surgery during the resuscitative (acute) phase of the injury.
- Others perform the surgery in the first 4-7 days after the injury.



Figure 28-24: Burned hands with third degree burn with multiple escharotomies performed

Anesthetic Management of a Burned Patient

Preoperative Management:

After resuscitation and burn assessment, the following preoperative assessments are important.

1) Preoperative Assessment of the Pulmonary System: for example:

- **Wheezing or rhonchi** indicating pneumonia.
- **Arterial blood gases.**
- Aggressive **pulmonary toilet** to facilitate clearing of secretions.
- If the patient is already intubated, it is important to **note the ventilator settings,** as usually high minute volumes and high peak airway pressures are required due to the decreased compliance from the inhalational injury, pneumonia, and circumferential contracting eschar around the chest wall. Many old anesthesia ventilators cannot generate sufficient volumes or pressures to ventilate these patients adequately; therefore, special ventilators should be prepared.

2) Preoperative Assessment of the Cardiovascular System:

Preoperative assessment is important to detect the **efficacy of resuscitation** for example hemodynamic stability and adequacy of urine output.

3) Preoperative Assessment for Electrolyte Imbalance.

4) Preoperative Assessment of the Other Effects of Burn:

Such as infection and septic shock, coagulation system, stress ulcer, and effects of electrical burns.

5) Preoperative Patient Preparations:

• Large bore **i.v. cannula** and **cross-matched blood** should be prepared if excessive bleeding is suspected.
• On patient's transfer from the burn unit to the operating room, **hypothermia** may occur due to wet, bulky dressings causing large evaporative heat loss; so, these dressings should be changed frequently.

6) Premedications:

- Sedatives are avoided in critically ill patients with hemodynamic instability.
- Antibiotics are important.

Intraoperative Management:

Monitoring:

Besides the standard monitors, the choice of monitors is chosen according to the patient's medical condition.

- ECG: Its skin electrode will not stick to the burned area (due to lipolysis from the burned area or antibiotic cream); therefore, it can be replaced by:
  - needle electrodes,
  - esophageal leads, or
  - foam electrodes, which are secured in the burn eschar with a skin stapler (without risk of the needle sticking to the patient or staff).
- Arterial line for invasive arterial blood pressure and blood gases.

Non-invasive blood pressure monitor with a sphygmomanometer cuff in patients with extensive burns can be misleading. In a burned limb- or in an unburned limb in which massive edema develops, Korotkoff sounds may be progressively attenuated, falsely implying hypoperfusion and hypotension.

- Central venous pressure.
- Pulmonary artery catheter.
- Urine output.
- Peripheral nerve stimulator.
- Temperature electrode.
- Serum lactate.
- Intramucosal pH.

Induction and Intubation:

Great care should be taken especially in case of burns of the head and neck.

a- **Awake intubation** (oral or nasal) is indicated in **cooperative patients** by a fiberoptic bronchoscope. Nasal intubation is usually used especially if prolonged postoperative intubation is planned because:

- It is easily secured in place.
- It is better tolerated by the patient.
- It allows oral hygienic care.

b- **Inhalational induction** is indicated in **uncooperative patients** with suspected difficult intubation.

Problems during Intubation:

- The **range of movement in the neck and tempro-mandibular joint** may be grossly restricted; therefore, laryngoscopic intubation may be impossible.
- The **raw painful tissues** may prevent application of **the facemask**.
- **Tracheostomy is undesirable** due to the increased risk of spread of **infection** to the damaged skin.
- **Suxamethonium is avoided** in burned patients with muscle damage because suxamethonium may **increase the release of K^+** into the circulation reaching very dangerous levels (10 mEq/L has been reported). This may cause cardiac arrest due to presence of **extra-junctional acetylcholine receptors** that increase the sensitivity of the muscle membrane. The period of increased sensitivity (and thus, avoidance of suxamethonium) is unclear. It differs from centers to others:
  - Some centers avoid suxamethonium from the **1st 24-48 hours up to healing** with a maximum limit of 2 years.
  - Other centers avoid suxamethonium from the **4th day up to 10 weeks** only after thermal injury.

  This effect is present **irrespective of the degree or the extent of burn** as it can occur in patients even with < 10 % burns.
- **There is a difficulty in securing the endotracheal tube in place;** therefore,
  - Suspend the anesthetic breathing system form the ceiling,
  - Use an umbilical tape to tie the tube in place, or
  - Wire the tube to the upper teeth.

Maintenance: according to the patient's hemodynamics:

O_2 + N_2O + **high dose opioid (during the acute phase) or volatile agents (during the subacute phase)** + muscle relaxants + a special mechanical ventilator.

- **Opioids**: They produce less myocardial depression; so, they are best used **in the acute phase**.
- **Volatiles**: They can be used **after the acute phase only** because:

- they produce marked myocardial depression.
- they increase arrhythmias especially if halothane is used with epinephrine-soaked bandages which are used to decrease bleeding.

- **Ketamine** infusions: can be used during **burn dressing** with special care for:
  - maintaining airway,
  - giving antisialagogue, and
  - giving diazepam to decrease hallucinations.
- **Muscle relaxants**: **Increase the dose** of non-depolarizing muscle relaxants due to:
  - Increased α_1 glycoprotein, which increases plasma protein binding of muscle relaxants.
  - Increased number of extra-junctional acetylcholine receptors which bind muscle relaxants without causing a block.
- **Mechanical ventilation**:
  - It is essential in severely burned patients due to the possibility of hypoxia (see above).
  - **Special ventilators** are needed that can provide high minute volumes (up to 30 L/min), high peak during pressure, and positive end-expiratory pressure (PEEP).

Intraoperative Problems and Considerations:

1- Increased Blood Loss: especially if the surgery is done for:
- A graft within more than a few days after the burn.
- Areas, which cannot be isolated by a tourniquet.

2- Hypothermia: is common due to:
- Evaporation from the burned area.
- Inability to constrict cut vessels and inability to decrease heat radiation.
- Effects of general anesthesia on the heat-regulating center.

Methods to decrease heat loss should be considered such as:
- Blood warmers to warm blood and i.v. fluids.
- Warming blanket.
- Covering of body areas not involved in the surgery.
- Gas humidification by a heated-humidified circuit.
- Ambient theater temperature at (27°C) and humidity of (50%).

3- Fluid management:
- Fluid resuscitation should be continued as before.
- Evaporative water loss from the wound typically peaks on the third postburn day and persists until the burn wound is healed or grafted.
- Insensible water losses may be estimated according to the following formula:

Insensible water loss (mL/h) = (25% + % of body surface area burned) x total Body surface area (m^2)

This formula, like the initial resuscitation formulas, is only an estimate, and replacement of evaporative water loss should be **guided by assessing the adequacy of hydration by monitoring serum osmolality and serum sodium.**

Extubation:

Before extubation, examine the larynx and pharynx because **edema** may be present around the base of the tongue producing respiratory obstruction after extubation. **Awake extubation** is mandatory if there is a possibility of inhalational injury.

Postoperative Management and Intensive Care Unit (ICU) Considerations:

Care during **patient's transport** to the ICU with standard monitors should be taken. ICU admission of a burned patient is usually needed for the following considerations:

1- Providing the initial care and completing the emergency resuscitative measures such as fluid resuscitation.

2- Providing the proper monitoring to assess adequacy of resuscitative measures and to detect and treat the possible complications.

3- Postoperative ventilation is needed in case of severe pulmonary affection.

4- Postoperative analgesia is important especially at sites of skin graft donor.

5- Prevention and treatment of complications such as:

a- **Infections**: such as wound infection, pneumonia, urinary tract infection, endocarditis, and sinusitis.
- Proper antibiotics according to culture and sensitivity test are important (**thrice-weekly cultures of sputum and the burn wound surface and twice-weekly culturing of urine and stools**).
- The most common organisms are all species of staphylococci, pseudomonas, and streptococci.

- The infection control committee should monitor infections occurring in the burn unit to identify changes in microbial prevalence, the incidence of infection, and evidence of cross contamination.

b- **Inhalational injury**: see above.

c- **Renal failure**: see above.

d- **Systemic infection response syndrome (SIRS) and disseminated coagulopathy** (DIC).

6- Nutrition and hyper-metabolic status:

- **The level, cause, and clinical picture** of hyper-metabolic status are discussed above.
- **Estimation of caloric needs**: Many formulas exist for the estimation of caloric needs in thermally injured patients. These formulas are only a guide, but serial measurements by indirect calorimetry provide the most accurate determination of energy requirements for patients with major burns. These formulas are discussed in the chapter of "Intensive (Critical) Care".
- **Protein supply** should be higher than any other critically ill patients due to excessive protein catabolism. There are different methods to calculate protein supply such as:
  - Supplying 12-18 g of nitrogen/m^2 of body surface area,
  - Supplying 1.5-2 g of protein/kg of body weight, or
  - Supplying 1 g of protein/kg of body weight + 2 g/% of burn.
- **Route of nutrition administration:**
  - The **enteral route is preferred as soon as possible**, to preserve the mucosal function and integrity and **to prevent bacterial translocation**. The latter is discussed in more details in the chapter of "Intensive Care". The enteral route is used if the patient does not have ileus by either nasogastric or nasopharyngeal feeding. Patients with **burns exceeding 30-40%** of body surface area may not be capable of meeting nutritional goals by **oral intake** alone and supplementation **with any of the commercially available enteral formulas with an appropriate calorie-to-nitrogen ratio** may be used.
  - **Parenteral nutrition** is reserved for patients with prolonged ileus or conditions prohibiting effective gastrointestinal motility or absorption.

7- Wound care: as above.

8- Prevention of stress ulcers: is performed by prompt resuscitation and early enteral nutrition, besides the antihistaminic drugs.

9- Prevention of bed (pressure) sores and contractures: is performed by careful nursing and physiotherapy.

10- Postoperative psychological support may be needed for patients who have been grossly deformed or are with an amputated limb.

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NUTRITIONAL DISEASES & INBORN ERRORS OF METABOLISM

29

- Nutritional diseases
  - Obesity
  - Eating disorders
    - Anorexia nervosa
    - Bulimia nervosa
    - Binge-eating disorder
  - Malnutrition and vitamin deficiencies
- Inborn errors of metabolism
  - Porphyria
  - Gout
  - Lesch-Nyhan syndrome
  - Disorders of carbohydrate metabolism
  - Disorders of amino acid metabolism

Nutritional Diseases

Obesity

Definitions It is a complex multifactorial chronic disease involving social, cultural, physiologic, psychologic, metabolic, endocrine, genetic, and behavioral components resulting in excess adipose tissues. Simply, obesity occurs when net energy intake exceeds net energy expenditure over a prolonged period of time.

Body Mass Index (BMI) or Quetelet's Index:

The name Quetelet's index is after the Belgian statistician, Adolphe Quetelet, published in 1842.

$$\text{BMI} = \frac{\text{Body weight (kg)}}{\text{Height square } (m^2)}$$

For example, a patient's body weight is 100 kg and the height is 1.7 meter tall. BMI = $\frac{100}{1.7^{\ 2}}$ = 34.6 kg/m^2

Values of BMI: BMI differs according to sex of the patient as follows:

Category	BMI (kg/m^2)
Anorexia	< 17.5 in men or women
Underweight	17.6 to 19.0 in women 17.6 to 20.6 in men
Ideal (Normal) Weight	19.1 to 25.8 in women 20.7 to 26.4 in men
Marginally Overweight	25.9 to 27.2 in women 26.5 to 27.8 in men
Overweight	27.3 to 32.3 in women 27.9 to 31.1 in men
Obese class I	32.4 to 34.9 in women 31.2 to 34.9 in men
Obese class II (Severe Obesity)	35.0 to 39.9 in men and women
Extreme Obesity, sometimes called class III (**morbid obesity**; an old term)	≥ 40 to 49.9 (or ≥ 35 with significant co-morbid conditions)
Super Obese	≥ 50 to 59.9
Super Super Obese	≥ 60

Sometimes, an approximate non-sex specific simple system is used as follows:

Category	BMI (kg/m^2)
Healthy (Normal) Weight	18.6 to 24.9
Overweight	25 to 29.9
Obesity	30 to 34.9
Severe Obesity	35 to 39.9
Extreme (Morbid) Obesity	40 to 49.9
Super Obesity	≥ 50

Older Definitions

Overweight: was formerly defined as a body weight of up to 20% greater than the predicted ideal weight.
Obesity: was formerly defined as a body weight more then 20% greater than the predicted ideal weight.
Morbid obesity: was formerly defined as a body weight of twice the ideal body weight.
These old definitions are inaccurate and abandoned.
N.B.:

Ideal Body Weight (IBW):

It describes the weight that is statistically associated with maximum life expectancy. Normal weight ranges between 10% above and below IBW. IBW can be detected by either:

- Actuarial tables depending on height, sex, and body frame size.
- **Broca's index** = Height in cm – 100 for males.
  Or = Height in cm – 105 for females.

Total Body Weight (TBW): includes:

a- Lean Body Weight (LBW):

It includes the weight of the muscles, bones, tendons, ligaments, and body water. It is normally 80% of the total body weight in males and 75% of the total body weight in females. LBW can be calculated using the following formulas (of James):

- Lean body weight (men) = (1.10 x weight in kg) – 128 x (weight^2/(100 x height in meter)^2)
- Lean body weight (women) = (1.07 x weight in kg) – 148 x (weight^2/(100 x height in meter)^2)

In general, LBW is equal to **IBW plus 20-40%.**

b- Fat Weight:

It includes the weight of adipose tissues. Obesity occurs when fat weight exceeds 30% of the TBW.

Triceps Skin-fold Thickness:

It is an alternative system to detect the obesity. A triceps skin-fold thickness of **more than 23 mm in men** and **more than 30 mm in women** is defined as **obesity**.

Distribution of Fat

Central (Android or Cushingoid) Pattern:

Fat is mainly around the **upper abdomen and viscera (waist)** and the individual has **an apple shape**. It is more found **in men**. This type is associated with **more medical and metabolic complications** (metabolic syndrome).

Peripheral (Gynecoid or Gluteal) Pattern:

Fat is mainly around the **gluteofemoral and lower abdomen regions** and the individual has **a pear shape**. This type is associated with **less medical and metabolic complications** (figure 29-1).
Therefore, **the waist circumference** is used nowadays to indicate the presence of central obesity, which is diagnosed when waist circumference is **> 102 cm (40 inch) in men and > 88 cm (35 inch) in women.**

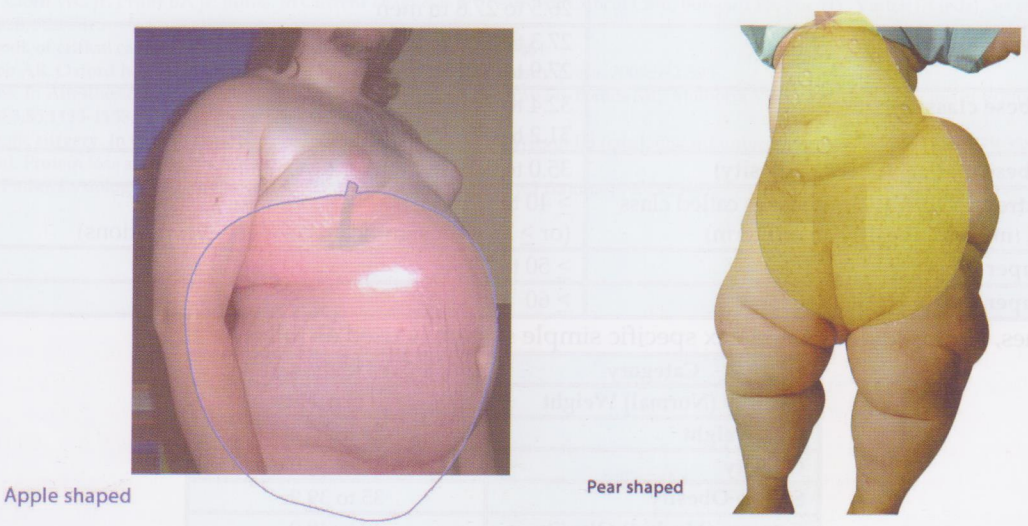


Figure 29-1: The central (left) and peripheral (right) patterns of obesity

Pathogenesis and Mechanisms of Obesity

• As defined before, obesity is a complex multifactorial chronic disease involving social, cultural, physiologic, psychologic, metabolic, endocrine, genetic, and behavioral components resulting in excess adipose tissues.

• The primary form in which potential chemical energy is stored in the body is fat (triglyceride). The high caloric density and hydrophobic nature of triglycerides permits efficient energy storage without adverse cosmotic effects. The amount of triglyceride in adipose tissues is the cumulative sum of the differences between energy (food) intake and energy expenditure (resting metabolism and physical activity) over time. If daily energy intake exceeds energy expenditure by 2%, the cumulative effect after 1 year is approximately a 2.3 kg increase in body weight.

• Surplus calories are converted to triglycerides and stored in adipocytes. This storage is regulated by the enzyme lipoprotein lipase. The activity of this enzyme varies in different parts of the body, being more active in abdominal fat and less active in hip fat. Because men tend to accumulate abdominal fat, which is broken down by the more active form of lipoprotein lipase, they generally lose weight more readily than women, who accumulate hip fat.

• When triglycerides are deposited in fat cells, the cells initially increase in size until the maximum size is reached, at which point the cells divide. Moderate degrees of obesity (BMR < 40) are likely to result in increased fat cell size, whereas extreme obesity (BMR > 40) is likely to result in adipocytes proliferation.

Clinical Manifestations (Anesthetic Problems and Considerations)

There is an increased metabolic rate and a large sized body.

1) Respiratory Effects:

1- Picture of Restrictive Lung Disease:

There is a decrease in inspiratory reserve volume, expiratory reserve volume, functional residual capacity (FRC), vital capacity, and total lung capacity due to:

- **Decreased chest wall compliance** (but lung compliance may remain normal) by excessive adipose tissue over the thorax. This increases the work of breathing, which is mainly diaphragmatic.
- **Increased abdominal mass**, which **forces the diaphragm upwards.** It is accentuated by supine, trendelenburg or lithotomy positions.

General anesthesia will accentuate these changes such that a 50% decrease in FRC occurs in obese anesthetized patients compared with a 20% decrease in non-obese individuals.

2- Ventilation/Perfusion Mismatching (i.e., increased intra-pulmonary shunt) due to:

- **Decreased ventilation:** Compression of the lung by the external adipose tissues decreases ventilation and FRC below the closing capacity (the closing capacity is not changed or increased); therefore, some alveoli will close during normal tidal volumes. This collapse of alveoli is avoided by positive end expiratory pressure (PEEP) and increased FiO_2.
- **Increased perfusion** caused by an increase in the cardiac output and blood volume.

N.B.: Normally, the FRC acts as a buffer between the lung's volume and the closing volume i.e., FRC prevents the lung from falling into the closing volume range. After exhalation of normal tidal volumes, there is plenty of air remaining in the lung, preventing it from shrinking to the closing volume. In morbidly obese patients, the lung is compressed from external adipose tissue; so, the lung's volume shrinks down to its closing volume, and more alveoli are collapsed.

3- Dead Space Volume/ Tidal Volume Ratio (V_D/V_T):

The V_D/V_T ratio is often **less than the normal** due to the increased tidal volume and the unchanged dead space. This ratio can be estimated by the Bohr equation = $V_D/V_T = (PaCO_2\text{-}PÉCO_2)/PaCO_2$

N.B.: $PÉCO_2$ = Mixed expired CO_2 tension.

4- Obstructive Sleep Apnea and Hypopnea Syndrome (OSAHS):

It is a sleep disorder. It is either:

- **Obstructive sleep apnea (OSA):** is defined as complete cessation of airflow more than 10 seconds more than 5 times/hour of sleep, associated with oxygen desaturation and **disturbed sleep.**
- **Obstructive sleep hypopnea (OSH):** is defined as a decreased airflow more than 50%, which is repeated more than 15 times/hour of sleep, associated with oxygen desaturation and disturbed sleep.

Both OSA and OSH are discussed in more details later.

Obesity-Hypoventilation Syndrome (OHS):

- OHS is the long-term consequence of **severe OSA**. It occurs in **extremely obese patients** (8% of all obese patients).

• OSA is initially limited to nocturnal sleep with correction of respiratory acidosis occurring during waking hours. As the OHS develops, there is evidence of nocturnal alterations in the control of breathing manifesting as central apneic events (apnea without respiratory efforts). These **nocturnal episodes of central apnea** reflect progressive insensitivity of the respiratory centers to nocturnal hypercarbia. The OHS is also associated with **obesity and chronic daytime hypoventilation (with hypoxemia and hypercapnia)**, not related to pulmonary diseases.

Pickwickian Syndrome (PS):

• It is **a severe OHS** characterized by **obesity, daytime hypoventilation (with hypoxemia and hypercapnia), cyanosis induced polycythemia, daytime hyper-somnolence, respiratory acidosis, pulmonary hypertension, and right-sided heart failure (i.e., cor pulmonale).**

In OHS and PS postoperative ventilation is usually needed after abdominal surgery and arterial blood gases are essential.

N.B.: Pickwickian syndrome was named by **Burwell in 1956** as he felt that the first adequate description of this syndrome had been made in 1837 by **Charles Dickens** in the Posthumous Papers of the **Pickwick club** in which he described a boy named Joe with the same features of this syndrome.

$PaCO_2$ levels:

• **In young, active subjects**: Normal values are **around 35 mm Hg** due to alveolar hyperventilation in response to a hypoxic drive.

• **In OSAHS (OSA and OSH): Periodic, nocturnal, hypercarbia** due to alveolar hypoventilation with normal daytime values.

• **In OHS and PS: Daytime, or constant, hypercarbia** due to alveolar hypoventilation.

2) Cardiovascular Effects:

1- There is **increased cardiac output** (0.1 L/min/kg of excess adipose tissue) due to an increase in the stroke volume and a greater increase in the heart rate. This increases the work of the heart.

There is also **increased blood volume** secondary to polycythemia.

Both the increase in cardiac output and blood volume **increase the arterial blood pressure** and **produce congestive heart failure**.

2- There are **conduction defects** due to fatty infiltration of the conduction system.

3- There is an increased incidence of **coronary artery disease, atherosclerosis, and systemic and pulmonary hypertension**.

4- **In Pickwickian syndrome,** there is **pulmonary hypertension and cor pulmonale** due to:

• Increased pulmonary blood flow.

• Hypoxic pulmonary vasoconstriction.

5- There is **an increased** incidence of **deep venous thrombosis (DVT),** double that of non-obese individuals due to: • chronic limited mobility,

• polycythemia, which increases blood viscosity, and

• increased abdominal pressure, which causes venous stasis.

3) Gastrointestinal Effects:

1- Increased incidence of **regurgitation** and **aspiration pneumonia** (although some researches fail to show this increased incidence in obese patients) due to increased possibility of:

• Hyper-acidic gastric fluid; 90% of fasting morbidly obese patients exceed Mendelson's criteria, a gastric volume of greater than 0.25 mL/kg total body weight with a pH less than 2.5.

• Hiatus hernia.

• Gastroesophageal reflux. Recent researches showed that barrier pressure at the gastroesophageal junction is the same in obese and non-obese individuals.

• Poor gastric emptying (it is controversial as some researches indicate presence of increased gastric emptying in obese patients and other researches have showed no differences in obese and non-obese individuals).

• Linear increase in intra-abdominal pressure with increasing body weight.

Recent researches have showed that morbidly obese patients following standard nothing by mouth guidelines and without significant gastrointestinal reflux disease are most likely not "full stomach".

2- Increased incidence of **hepato-biliary diseases** such as:

• Fatty infiltration of the liver (usually not affecting the liver function). There is increased biotransformation (reductive pathway) of volatile agents.

• Cholelithiasis (gall bladder stones).

- Hepatitis.
- Intra- and extra-hepatic cholestasis.

4) Metabolic Effects:

1- **There is an increased metabolic rate** in proportion to the increased body weight resulting in **increased O_2 consumption and CO_2 production**, which result in hyperventilation.
2- **Type II diabetes mellitus,** hyper-insulinoma and increased insulin resistance.
3- **Hypercholesterolemia, hyperlipidemia, and hypertriglyceridemia.**
4- **Metabolic syndrome:**

Diagnosis: (according to the International Diabetes Federation)
There must be central obesity (by waist circumference, as above) with 2 or more of the following criteria:

- **Increased serum triglycerides** ≥ 150 mg/dL (1.7 mmol/L) or specific treatment for this lipid abnormality.
- **decreased high-density lipoprotein cholesterol (HDLC)** < 40 mg/dL (1.0 mmol/L) in men or < 50 mg/dL (1.3 mmol/L) in women, or specific treatment for this lipid abnormality.
- **Hypertension** (systolic blood pressure ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg) or on treatment for previously diagnosed hypertension.
- **Diabetes mellitus type II** (fasting serum glucose ≥ 110 mg/dL) or on treatment for previously diagnosed diabetes. There is insulin resistance and resultant hyper-insulinemia.

Other components of the have been suggested, e.g., **hyper-homocysteinemia, micro-albuminuria, hyper-uricemia, elevation of inflammatory markers, and increased prothrombotic and antifibrinolytic factors.** It is also suggested that **non-alcoholic fatty liver disease** is the hepatic manifestation of the metabolic syndrome. Most recently, impaired lung function was found to be associated with the metabolic syndrome.

N.B.: Lipid triad (dyslipidemia) includes in addition to the above 2 lipid abnormalities, increased small dense low-density lipoprotein cholesterol (LDL-C).

Cause: The cause of metabolic syndrome is **unknown**, but it is believed that the breakdown products of the visceral (central) fat are delivered directly into the portal circulation where they produce a metabolic imbalance.

Risk factors: They include old age, menopause, genetic predisposition, race (more common among blacks and Mexican Americans than among Caucasians), disturbances in sex hormones (e.g., polycystic ovary syndrome (POS), hyper-androgenism in pre- and postmenopausal women), energy excess (higher carbohydrate, high fat, low food fiber, high meat intake), family history (diabetes, hypertension, obesity), overweight, life styles (tobacco use, alcohol consumption, physical inactivity, snoring and obstructive sleep apnea syndrome, psychosocial and personality factors (lower social class, difficulty in coping with stress, higher hostility level).

Treatment: Once a diagnosis of the metabolic syndrome is made, the future management of the condition should be aggressive and uncompromising in its aim to reduce the risk of cardiovascular disease and type 2 diabetes. Patients should undergo a full cardiovascular risk assessment (including smoking status) in conjunction with the following:

- **Primary intervention**:
  - Healthy lifestyle promotion. This includes:
    - Moderate calorie restriction (to achieve a 5–10 per cent loss of body weight in the first year).
    - Moderate increase in physical activity.
    - Change in dietary composition.
- **Secondary intervention**: In people for whom lifestyle change is not enough and who are considered to be at high risk for cardiovascular disease, drug therapy may be required to treat the metabolic syndrome. These drugs are mainly for **treatment of dyslipidemia, hypertension, and diabetes mellitus.**

5) Airway Problems:

Morbid obesity is associated with increased possibility of:

- **Difficult mask ventilation**.
- **Difficult and failed intubation**.
- **Airway obstruction** with light to moderate sedation.

These effects are due to the following anatomic changes:

- **Deposition of adipose tissue in** the following areas:

- **Lateral pharyngeal wall, uvula, tonsillar pillars, the tongue (causing a large tongue), and the aryepiglottic folds**, causing a decrease in the pharyngeal area.
- **External to the upper airway (lateral parapharyngeal fat pads, or jowls)**, extrinsically compressing the airway.
- **The hypopharyngeal area**, acting as a ball valve, obstructing the upper airway, and interfering with the line-of-sight at direct laryngoscopy.
- **The pretracheal area**, pushing the hyoid bone posteriorly into a less favorable position, causing the epiglottis to partially override the glottic entrance, worsening the laryngoscopic view.

• **Alteration in the shape of the pharynx** from an ellipse with the long axis lateral transverse to an ellipse with long axis anterior-posterior.
• **Decreased mandibular and cervical mobility.**
• **Short neck.**

6) Other Problems:

• Osteoarthritis; care is taken during **positioning.**
• Increased difficulty in **surgical techniques**.
• Increased difficulty in **local anesthetic techniques**.
• Increased difficulty in achieving **venous access**.
• Increased **blood loss**.
• Increased **wound infection and wound dehiscence**.
• Increased **bed sores**.
• Increased **neoplasia** as breast or colon.

7) Obesity with Pregnancy:

• There is **addition of the physiologic changes of pregnancy to the pathologic changes of obesity.** Physiologic changes of pregnancy are discussed in the chapter of "Obstetrics".
• There is increased incidence of **preeclampsia and aorto-caval compression**.

8) Obesity with Laparoscopic Procedures:

Both morbid obesity and pneumo-peritoneum during laparoscopic procedures are associated with increased intra-abdominal pressure, which produces **respiratory, cardiovascular, and gastrointestinal effects**. These effects are **exaggerated and increased** in extremely obese patients than normal-weight patients. Healthy morbidly obese patients can tolerate these changes relatively well. The effects of pneumo-peritoneum are discussed in chapter "Laparoscopic Surgery".

Treatment of Obesity

1) Control of Energy Balance:

• Decrease the caloric intake by **dietary control** (i.e., decrease fat and sugars and increase vegetables).
• Increase the caloric expenditure by increasing the physical activity (**exercise**).
• **Behavioral modifications** are advised.
• **Pharmacological treatment:** Most of them are appetite suppressants.

Drugs used in Obesity	Implications for Anesthesia
1- Diethyl-proprion	Pulmonary hypertension, psychosis.
2- Fenfluramine (*Pondimin, Ponderax* and *Adifax*): a serotonin reuptake inhibitor	Pulmonary hypertension.
3- Fluoxetine (*Prozac, Sarafem*): a serotonin reuptake inhibitor	Diarrhea, nausea, headache, dry mouth, bradycardia, bleeding, seizures, hepatotoxicity, and extra-pyramidal effects.
4- Mazindol (*Mazanor, Sanorex*)	Pulmonary hypertension, atrial fibrillation, syncope.
5- Metformin (*glucophage*)	Metabolic acidosis.
6- Silbutramine (*Miridia or Sibotrim*); a serotonin and norepinephrine reuptake inhibitor	Hypertension, tachycardia, and arrhythmias.
7- Phentermine; a serotonin reuptake inhibitor	Cardiopulmonary problems.
8- Phenyl-propanolamine (*PPA; Accutrim*)	Hemorrhagic stroke.
9- Orlistat (*Xenical or Orli*)	A lipase inhibitor that acts in the gastrointestinal tract and is not absorbed. It causes diarrhea, fat-soluble vitamin (A, D, E, K) deficiencies.

These drugs should be **discontinued 2 weeks before anesthesia.**

• **Dietary supplement/herbal products** used for weight reduction:

Dietary Supplement/Herbal Products	Implications for Anesthesia
Chitosan (*Protasan*)	No adverse effects.
Chromium	No adverse effects.
Hydroxy-citric acid (Garcinia Cambogia)	No adverse effects.
Ephedra (Ephedrine, Ma Huang)	Hypertension, psychiatric disease, autonomic dysfunction, gastrointestinal symptoms.
Pyruvate	Restrictive cardiomyopathy.

2) Surgical Procedures (Bariatric Surgeries):

1- Restrictive Procedures: They include:

a- **Adjustable gastric banding:** It is the **most common performed** Bariatric procedure. The surgery entails the placement of an adjustable band around the upper end of the stomach, creating a small pouch and restrictive stoma that slow the passage of food into the distal gastrointestinal tract, without cutting of, or entry into, the stomach. The gastric band is adjusted after surgery by injection into a subcutaneous port placed at the time of surgery.

b- **Stapling gastroplasty:** It is reduction of the stomach to a small gastric pouch (about 100 mL) with a narrow stoma.

Both gastric banding and stapling gastroplasty can be performed as laparoscopic procedures.

c- **Sleeve gastrectomy:** It is excision of a large part of the stomach leaving a small narrow tubular canal that allows passage of the food.

d- **Intragastric balloon insertion:** by the fiberoptic scope.

These procedures produce **the least nutritional and metabolic complications** because no part of the small intestine is bypassed.

2- Intestinal malabsorptive procedures: They include the bilio-pancreatic diversion with/without duodenal switch and distal gastric bypass. **Partial gastrectomy** is done leaving **a large gastric pouch** and **the small intestine is divided** at the ileum, 50-100 cm proximal to the ileocecal valve. **The gastric pouch is then anastomosed with the distal limb** of the divided small intestine, producing a gastro-ileostomy **through which the food passes** bypassing a considerable length of the small intestine to decrease its adsorption. **The remaining proximal divided intestinal limb** containing the bile and pancreatic juices (**bilio-pancreatic conduit**) is **anastomosed to the side of the distal ileum** to deliver the bilio-pancreatic juice to the passage of the food to allow its digestion.

This procedure is associated with **the greatest risk of nutritional and metabolic complications** because of the extensive bypassing of small intestine (including the entire jejunum). These procedures are nearly obsolete nowadays.

3- Roux-en-Y gastric bypass procedure:

This procedure combines **both restrictive and malabsorptive component**. The stomach is divided into a small proximal pouch and a large distal gastric pouch. The small intestine is divided at the jejunum. **The proximal small gastric pouch is anastomosed to the distal jejunum** where the food passes through the ileum allowing good food absorption. **The distal stomach, duodenum, and proximal jejunum** (containing bilio-pancreatic juice) **are bypassed**, decreasing the absorption of nutrients, but the duodenum is **connected to the distal jejunum** to deliver the bilio-pancreatic juice to the food reaching the distal jejunum. This procedure produces **less nutritional and metabolic complications than the intestinal malabsorptive procedures** because the food passes through the distal jejunum and all the ileum.

Complications of Bariatric surgeries:

- Anastomotic (suture line) leak or rupture.
- Stomal stenosis or anastomotic stricture.
- Gastric ulcer or prolapse.
- Esophagitis.
- Repeated nausea and vomiting.
- Nutritional and metabolic complications such as vitamin B_{12}, folate, iron, and protein deficiencies.

Other surgical procedures:

1- Temporary dental splinting.

2- Dermolipectomy and liposuction are performed to remove only a small proportion of body fat.

Anesthetic Management

Preoperative Management:

1- Preoperative Assessment by history, examination, and **full investigations** of the respiratory, cardiovascular, metabolic systems, hematology, and airway should be performed as above. The problems in these systems should be detected and managed.

2- Preoperative Continuous Positive Airway Pressure (CPAP) or Noninvasive Positive Pressure Ventilation:

- CPAP may improve the preoperative condition of the patients who are at increased perioperative risk from OSA. 3 months of CPAP treatment may reverse OSA-induced cardio-vascular dysfunction and the metabolic syndrome. CPAP protects the patient against airway obstruction during sleep by pneumatically splinting the oro-pharynx.
- CPAP is titrated and given to the patient either in the 2nd half of the first night of the sleep study or on a 2nd separate night of a sleep study (see later) to determine the level of CPAP that causes a significant decrease in the apnea and hypopnea and produces patency of the airway.

3- Premedications:

Avoid intramuscular injections because they usually cause intra-fat injection, leading to unpredictable absorption. **I.v. or oral route is more suitable** for premedications.

N.B.: Intramuscular injections should be avoided in the following cases:

- Morbidly obese patients due to unpredictable absorption.
- Blood diseases e.g., hemophilia due to hematoma formation.
- Febrile children due to possibility of poliomyelitis.
- Tetralogy of Fallot due to crying of the child, which induces a hyper-cyanotic spill.

The following premedications can be given:

1. Sedatives:
   - In mild obese patients, slight sedation is allowed.
   - In OSAHS patients, no sedation is allowed.
2. Prophylaxis against aspiration such as antacids, H_2 blockers, or metoclopramide.
3. Prophylactic antibiotics.
4. Prophylactic anticoagulants against DVT.

Intraoperative Management:

Monitoring:

Besides the standard monitors, the choice of the monitors depends on the patient's medical condition.

- **Non-invasive blood pressure:** The **suitable cuff size** should be chosen because too small cuffs will overestimate the true blood pressure. The **length of the cuff bladder** should equal at least **80% of the measured arm circumference or, preferably, the entire arm** and the **width of the cuff bladder** should equal at least **40% of the measured arm circumference at the midpoint of the upper arm.**

Sometimes, a regular sized cuff can be used on the forearm or the wrist of the patient.

- **Invasive blood pressure** and **arterial blood gases.**
- **Central venous pressure (CVP) and pulmonary artery pressure (PAP) catheters:** The increased intra-abdominal and/or intra-thoracic pressures may be transmitted leading to elevated CVP and PAP, although there is hypovolemia.

Patient Position:

- **Ramped (or stacked) sniffing position:** By using multiple blankets or foam wedges, **the upper back should be elevated** relative to the abdomen with **the head in a sniffing position.** This position is optimal for airway management, preoxygenation, and even during trans-portation.

Sniffing position alone can be used in morbidly obese patients to facilitate intubation but a high pillow (s) is needed. To confirm proper positioning, view the lateral side of the patient; the head should be above the horizontal plane of the upper chest, or **a horizontal plane between the sternal notch and the external auditory meatus** is established. This position improves pulmonary mechanics and improves the alignment from mouth to glottic opening during intubation (figure 29-2).

- Careful positioning is needed as the patient **may fall down** especially in abnormal positions such as anti-trendelenburg position.
- Very obese patients may need **special operating tables** (as most operating tables can carry 120-200 kg only). Some clinicians can use **two regular tables joined together**.

• Particular care should be paid to **protecting pressure areas** because **pressure sores and neural injuries** such as brachial plexus, sciatic and ulnar nerve injuries are more common in this group, especially in the super obese and any obese patient with diabetes. **Rhabdomyolysis of the gluteal muscles** may occur leading to renal failure in morbidly obese patients, who were supine, assumed to be the result of poor perfusion of adipose tissue.



Figure 29-2: Three morbid obese patients with a very huge body and short neck in very high sniffing position although the external auditory meatus is still not in the same horizontal level of the sternal notch

Choice of Anesthesia:

A) Regional Anesthesia: with the following precautions:

- It is **more difficult** in obese patients to identify landmarks and needs longer needles.
- **Spontaneous ventilation** is difficult to be maintained in the supine position.
- **Decrease the dose** for epidural or subarachnoid block by 20-30% less than the ordinary doses due to:
  - presence of epidural fat and
  - distended epidural veins due to increased intra-abdominal pressure.

Combined continuous epidural (lumbar, thoracic, or cervical) anesthesia **with light endotracheal general anesthesia is recommended** because:

1. They decrease the stress on the cardiovascular system during surgery resulting in more stable hemodynamics (i.e., decreased blood pressure, heart rate, and systemic vascular resistance).
2. This method avoids the usage of opioids or potent inhalational agents.
3. There is rapid postoperative emergence causing early extubation.
4. It allows postoperative analgesia without respiratory depression.

B) General Anesthesia:

Generally, general anesthesia with a secure airway is preferable to deep sedation without an airway even with a superficial procedure.

Induction and Intubation:

• **Good preoxygenation** is essential with 100% O_2 **in the head-up tilt position** to obtain a 99-100% SaO_2 for: ▫ at least 3-5 minutes, which allows a 6.5 minute apnea for 90% SaO_2 (preferred) or
▫ at least 4-5 maximal breaths (vital capacities), which allows a 3.5 minute apnea for 90% SaO_2.
Preoxygenation is very essential because:
▫ Rapid desaturation occurs during periods of apnea in obese patients as there is a small intra-pulmonary store of O_2 (i.e., small FRC), which is rapidly consumed due to the high metabolic rate.
▫ Also, the tidal volume may fall below the closing volume of the small airways, leading to atelectasis.
▫ Difficult intubation is suspected needing a longer time.

• Continuous positive airway pressure **(CPAP) 10 cm H_2O** can be applied for **5 minutes before induction** of anesthesia. This is followed by positive end-expiratory pressure **(PEEP) 10 cm H_2O via the facemask before intubation.** This is more efficient in decreasing atelectasis.

• **All equipment for difficult intubation** (e.g., laryngeal mask airway or combi-tube) should be available.

• Methods of induction and intubation are chosen according to the patient's condition:
a- **Awake intubation** in **cooperative patients** is done by fiberoptic bronchoscopy if difficult intubation, airway obstruction, or aspiration is suspected.
b- **Inhalational intubation** in **uncooperative patients** is done if difficult intubation is suspected.
c- **Rapid sequence induction and intubation** is chosen if easy intubation without airway obstruction is suspected, but there is a risk of aspiration.
In an elective, fasting morbidly obese patient with no other significant risk factors, the need for rapid sequence induction with cricoid pressure to prevent regurgitation and aspiration is debatable.
d- **A tracheostomy** is mandatory before any surgery that involves the base of the tongue, although tracheostomy may be difficult in markedly obese patients with short necks.

• The criteria for the **best intubation attempt** should be fulfilled as the sniffing position, optimal external laryngeal manipulation…etc. Best intubation attempt is discussed in chapter "Airway Management".

• **Succinylcholine**: **The dose** should be **increased** to (1.2-1.5 mg/kg) due to the high pseudo-cholinesterase activity in obese patients.

• There may be **difficulty in auscultating breath** sounds; therefore, **$ETCO_2$ is essential.**

Drug Dosing in Obese Patients:

Drugs are dosed in the morbidly obese on the basis of their lipophilicity:

Lipophilicity	Volume of Distribution	Calculation of Doses	Examples
Highly Lipophilic Drugs	Increased for obese individuals relative to normal weight individuals.	Total or actual body weight (TBW)	Thiopental, propofol (some consider LBW for initial doses and TBW for maintenance doses), benzodiazepines, fentanyl, sufentanil (some consider TBW for initial doses and IBW for maintenance doses), dexmedetomidine, succinylcholine, atracurium, and cisatracurium.
Exceptions of Lipophilic Drugs	Unchanged	Lean body weight (LBW), which is 20-40% of the IBW	Remifentanil
Weakly lipophilic or lipophobic drugs	Unchanged	Lean body weight (LBW)	Alfentanil, ketamine, vecuronium, rocuronium, morphine.

Some other authors recommend a clinically applicable approach, which is to calculate the **initial dose** of injected drug for administration to obese patients based on **IBW (reflect LBW)** rather than actual body weight. **Subsequent doses** are determined based on the pharmacological response to the initial dose.

Maintenance:

O_2, N_2O, volatile agents, muscle relaxants, and mechanical ventilation are usually used.

• O_2: should not be < 40% to avoid hypoxemia especially in the prone, trendelenburg, and lithotomy positions.

• Volatile agents: There is a general increase in hepatic biotransformation (metabolism)
▫ **Isoflurane, desflurane, and sevoflurane** are drugs of **choice** because they have very low hepatic biotransformation.

- **Avoid** those with high hepatic biotransformation (reductive pathway due to hepatic hypoxia) such as **halothane**, as it increases the incidence of halothane hepatitis and **methoxyflurane,** as it increases the incidence of nephrotoxicity (by increased fluoride ions).

N.B.: **Opioids should be avoided** because they are lipid soluble drugs; so, they are distributed to the large fat mass i.e., they have increased volume of distribution, which prolongs their action and increases their respiratory depressant action.

- Muscle relaxants:

All muscle relaxants can be used, but:

- **The dosage** should be based **according to the type of muscle relaxants** (as above).
- **Peripheral nerve stimulators** should be used to avoid over-dosage. The increased distance from the skin probe to the nerve **decreases the efficiency of nerve stimulator;** therefore, there may be no response to a train of four, but surgeons still complain of inadequate abdominal muscle relaxation (this is a controversial explanation as it may be due to light general anesthesia).
- Start with the smallest possible dose, then increase the dose according to the patient's need determined by the nerve stimulator.

- Mechanical ventilation:

- **Pressure controlled ventilation** is sometimes preferred by some authors than volume controlled ventilation. If volume controlled ventilation is used, **large tidal volumes (10-12 mL/kg ideal body weight** rather than total body weight) are needed to provide better oxygenation and CO_2 elimination and to prevent atelectasis, but they increase the risk of pneumothorax.
- **PEEP** (10 cmH_2O) may improve ventilation/perfusion matching and arterial oxygenation in obese patients, but **some authors avoid PEEP** due to the high airway pressure produced, resulting in:
  - Interruption of pulmonary small vessels blood flow in the upper parts of the lungs which are highly ventilated resulting in ventilation/perfusion mismatching.
  - Worsening of pulmonary hypertension, which decreases the cardiac output.
  - A decrease in the venous return, which decreases the cardiac output.
  - An increased incidence of barotrauma.

Therefore, PEEP may produce hypoxemia and hypercarbia.

Recovery and Extubation:

- **Ideally, awake extubation and recovery** are usually done while the patient is in **a head-up to sitting position** to decrease compression of the diaphragm by abdominal contents. An **oro-pharyngeal and/or a long naso-pharyngeal airway** should be in-situ and **2- or 3- handed ventilation** should be available.

Criteria of extubation should be **fulfilled** before removal of the tube such as return of the level of consciousness, muscle power (determined by a nerve stimulator), and acceptable hemodynamics, arterial blood gases, and respiratory mechanics. Criteria of extubation are discussed in more details in the chapter of "Airway Management".

If the patient was on **CPAP** (nasal or full facemask) preoperatively, then the patient should be on CPAP postoperatively.

- **If there is a suspicion about the ability of the patient to maintain his airway** without obstruction, the endotracheal tube should be removed over an **airway exchange catheter or fiberoptic bronchoscopy.** This allows re-intubation to be easy if needed.
- Sometimes **in extremely obese patients, the endotracheal tube is left in situ** to be removed later if mechanical ventilation is required postoperatively.
- **Airway obstruction** after extubation is very **common** in OSA patients **especially** those with oral or nasal surgery. If **nasal packing** is needed, it should be **around the nasopharyngeal airway** (creating a central conduit for gas exchange); otherwise, **negative pressure pulmonary edema** and **death from asphyxia** may occur.
- **Discharge from the post-anesthesia care unit (PACU):** Patients with OSA should be monitored in PACU for 3 hours more than the non-OSA patients, or for 7 hours after the last episode of airway obstruction or hypoxemia while breathing room air in an unstimulating environment before discharge to an unmonitored setting.

Postoperative Management:

1) Postoperative Analgesia:

Postoperative analgesia is mandatory in obese patients **especially those with thoracic or abdominal surgeries**. One of the following techniques can be used:

- Continuous epidural block (local anesthetics or opioids).
- Patient controlled analgesia with opioids.
- Non-opioid-regimens as ketolac, clonidine, dexmedetomidine, ketamine, magnesium, or lidocaine.

It is **better to avoid opioids**, but if used should be **in the smallest doses** with close observation of the patients to detect **respiratory depression**. The conventional intramuscular opioid injections should be avoided in obese patients.

2) Postoperative Complications:

1- **Postoperative Pulmonary Dysfunction:**

a- Hypoxemia (which lasts 4-6 days) is common especially in:

- Morbidly obese patients.
- Presence of preoperative hypoxemia.
- Surgery involving thorax or upper abdomen (especially vertical incisions) leading to inability to cough or clear secretions due to splinting pain.
- Residual effects of intraoperative and postoperative opioids.

b- In patients with OSAHS, a disturbed sleep pattern in the postoperative period is common as follows:

- **During the first 3 days postoperatively:** The pain is high and deep stage 3 and 4 non-rapid eye movement (NREM) and rapid eye movement (REM) sleep are often suppressed. This causes an increased analgesic need; so, the danger of life-threatening apnea during drug-induced sleep is increased.
- **In the next 3 days:** Deep REM sleep rebounds where the danger of life-threatening natural deep sleep-induced apnea is increased.

Therefore, increased analgesic need followed by increased duration of REM sleep increases the risk of prolonged apnea during sleep for about one week in postoperative OSA patients.

The following measures should be taken:

- **O_2 supplementation**: is needed by a nasal cannula or mask for 4-6 days **with continuous positive airway pressure (CPAP)**. CPAP should be applied **as early as possible** in the postoperative period because the time of sleep is unpredictable.
- **Sitting or semi-sitting positions:** are recommended as they cause unloading of the diaphragm increasing the FRC by 30% (which is already decreased postoperatively), so ventilation is improved.
- **Early mobilization.**
- **Early physiotherapy.**
- **Postoperative analgesia.**
- In pickwickian patients, controlled ventilation may be needed overnight in the 1st postoperative day.

2- **Increased deep venous thrombosis (DVT):** due to:

- Immobility.
- Polycythemia.
- Congestive heart failure.
- Increased fibrinogen level.

The measures that prevent DVT should be taken such as prophylactic subcutaneous heparin, elastic stockings…etc.

3- **Increased risk of pulmonary embolism.**

4- **Wound infection and dehiscence**.

Obstructive Sleep Apnea and Hypopnea Syndrome

Definitions:

Obstructive sleep apnea hypopnea syndrome (OSAHS) is a sleep disorder with the following criteria:

Obstruction	↓ in airflow > 10 seconds	Times/hour of sleep	↓ in O_2 saturation	Disturbed sleep	Daytime sleepiness
Obstructive Sleep Apnea (OSA)	100% i.e., cessation of airflow	> 5	> 4%	Yes	Yes
Obstructive sleep hypopnea (OSH)	> 50% i.e., a decreased airflow	>15	> 4%	Yes with snoring	Yes

Both OSA and OSH repeatedly disrupt sleep due to increased ventilatory effort-induced arousal, which in turn, causes daytime sleepiness and altered cardiopulmonary and cortical function.

N.B.: Sleep disorders may be grouped into the following types:

- Conditions associated with excessive daytime somnolence (e.g., OSA).
- Conditions with disorders initiating and maintaining sleep (e.g., insomnia).
- Circadian rhythm disorders (e.g., jet lag).

Incidence:

Obstructive Sleep Apnea (OSA) is present in:

24% of **men** detected by sleep studying methods (**4%** are **clinically symptomatic** OSA)
9% of **women** detected by sleep studying methods (**2%** are **clinically symptomatic** OSA).

Pathophysiology:

A) Normal Pharyngeal Muscle Activity:

- The three pharyngeal segments (**naso-, oro-, and hypo-pharynx**) are **collapsible** because the anterior and the lateral walls lack bony support. The contractions of the diaphragm against the high resistance offered by the nose during inspiration create a sub-atmospheric intra-airway pressure, which may narrow the collapsible segments of the pharynx.
- **Humans** are the **only mammals** who **have an oropharynx** (in all other mammals the tip of the uvula touches the tip of the epiglottis), which enables singing and speaking (the oropharynx between the uvula and epiglottis creates a chamber for resonance) but also causes OSA.
- Normally, obstruction of the airway is prevented during inspiration (especially during sleep) by contraction of:

1- **The tensor palatini**: It prevents airway obstruction by the soft palate at the **nasopharynx**.
2- **The genio-glossus**: It pulls the tongue anteriorly, to open the **oropharynx**.
3- **The hyoid muscles**: They pull the epiglottis forward and upward to prevent obstruction at the **laryngo- or hypo-pharynx** by the epiglottis.

B) Normal Sleep:

Sleep consists of 4-6 cycles of:

- **Non-rapid eye movement (NREM) sleep**: passes through 4 stages, with progressive increase in the depth of sleep and slowing of the EEG waves. It is followed by:
- **Rapid eye movement (REM) sleep**: It is one stage only (figure 29-3).

During (stage 3 and 4) of the deep NREM sleep and the REM stage
(they are called slow waves or deep sleep)

↓

A generalized loss of muscle tone with a decrease in
the rhythmic activity of the upper airway muscles occurs

↓

An increase in the upper airway resistance (UAR)

↓

The pharyngeal sub-atmospheric pressure generated
by a diaphragmatic contraction increases and the
pharyngeal pressure becomes more negative

↓

An increase in pharyngeal collapse especially of
the lateral walls which are the major pharyngeal site of
adipose tissue deposition in obese patients.
In 50-75% of OSA cases, the obstruction occurs in at least
two pharyngeal segments (the naso-pharynx and either the
oro-pharynx or laryngo-pharynx)

Figure 29-3: Pharyngeal collapse during sleep

C) Causes of why obesity *per se* may produce OSA and OSH:

1- There is **deposition of adipose tissues** into pharyngeal tissues; the uvula, the tonsils, the tonsillar pillars, the tongue, the aryepiglottic folds and most importantly, **the lateral pharyngeal walls**. This decreases the patency of the pharynx, which correlates well with the severity of OSA.

2- The patency of the pharynx is determined by:

• The trans-mural pressure across its wall (i.e., the difference between the extra-luminal and intra-luminal pressure).

• The compliance of the pharyngeal wall.

If the intra-luminal pressure (inspiratory airway pressure) and the compliance are constant, the remaining important factor of upper airway patency is the **extra-luminal pressure,** which is determined by the superficially located fat masses i.e., the upper airway is compressed externally. Therefore, the severity of OSA correlates well with the **increased neck circumference** than with general obesity.

3- **Weight gain** results in a significant increase in OSA severity, while weight loss results in a significant reduction in OSA severity.

Risk Factors of OSAHS:

a- In obese Patients:

• **Obesity** (BMI > 30 kg/m^2): It is the most important factor. 60-90% of patients with OSA are obese.

• **Excessive neck circumference due to excessive fat:** in men > 17 inches and in women > 17 inches (generally > 44 cm).

• **Male gender.**

• **Middle-age.**

• **Evening alcohol consumption or drug-induced sleep**, which decreases pharyngeal muscle tone.

b- In Non-Obese Patients:

• **Cranio-facial** and **oro-facial** abnormalities such as micrognathia and retrognathia because both often position the tongue in a relatively posterior position.

• **Nasal obstruction** of any etiology.

• **Large tonsils or tongue.**

• **Cartilaginous abnormalities** such as lingual tonsillar hyperplasia.

D) Arousal and Systemic Pathophysiology of OSA:

The systemic patho-physiological events are discussed in figure 29-4.

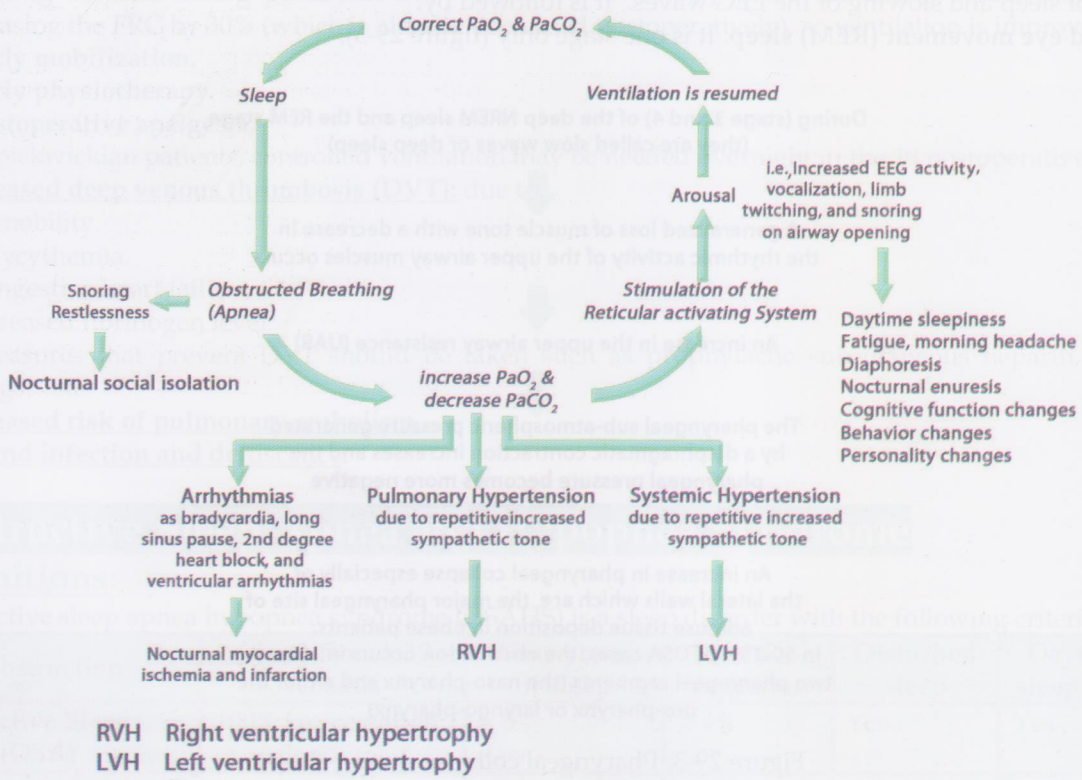


Figure 29-4: Pathophysiology of OSA

Causes of arousal during sleep apnea:

• Arterial hypoxemia.

- Hypercapnia
- Increased ventilatory effort (by hypoxia and hypercarbia).
- The increased ventilatory effort against an obstructed airway increases negative pressure in the airway.

Anyone, or all 4 causes together can be responsible for increased neural traffic in the reticular activating system and arouse the individual.

Causes of Death during Anesthesia:

1- Failure of intubation.
2- Respiratory obstruction soon after extubation.
3-Respiratory arrest after narcotic and sedative medications.

Differences between Obstructive and Central Apnea:

- **In OSA and OSH**, there is **breathing effort** but **no (or decreased) airflow;** the patient tries to breath (generates negative pressure in the chest), but fails to breathe. After several progressively harder attempts to breathe, the airway opens with a few deep breaths and then the ordinary breathing resumes.
- **In central sleep apnea,** there is **no breathing effort or airflow** i.e., no patient's trial to breathe and no generated negative pressure in the chest. After a variable pause, the patient begins to breathe with an ordinary effort.
- **In mixed apnea,** the patient starts out with a central apnea, which is followed by an obstructed apnea, which ends as described previously.

In a typical patient with moderate OSA, 85% to 95% of the apneas are obstructive, a few are central and a few are mixed.

Investigations:

A Full Sleep Study (Polysomnography):

It is performed in a sleep laboratory where nocturnal sleeping patterns are examined by monitoring many physiologic parameters.

Physiologic Parameter	Method of Study
1- The stage of sleep and arousal.	By electro-encephalogram (EEG).
2- NREM vs. REM sleep	By electro-oculogram (EOG).
3- Air flow or movement (the actual breathing)	By oral and nasal airflow sensors, microphones (for noise of snoring), and capnography.
4- The breathing effort	By esophageal pressure measurement and chest and abdominal movement (electromyography).
5- Pharyngeal muscle activity (genio-glossus and digastric muscles)	By submental electromyography.
6- Body position	By an infrared video camera.
7- Extremity movement	By extremity electromyography.
8- Hypoxia	By oximetry (pulse, ear, transcutaneous) and arterial blood gases analysis.
9- Cardiovascular changes	By non-invasive and invasive blood pressure, ECG, pulmonary artery pressure monitor.

Interpretation of the Sleep Study:

- **Apnea** is detected as no airflow > 10 sec.
  Hypopnea is detected as decreased airflow or tidal volume < 50% for > 10 sec.
- **In OSA and OSH**, there is **breathing effort** but **no (or decreased) airflow,** but **in central sleep apnea,** there is **no breathing effort or airflow**.
- **Apnea-hypopnea index (AHI)**: It is the total number of apneas and hypopneas per hour. It is used to define **the severity of OSA** as:
  - Values of 6-20 indicate mild OSA.
  - Values of 21-40 indicate moderate OSA.
  - Values of > 40 indicate severe OSA.

The severity of OSA is also determined by the loudness of snoring and movement during sleep (social problem), risk of arrhythmia and myocardial ischemia (decreased SpO_2), dual circulation hypertension and biventricular hypertrophy, and risk of death from a motor vehicle accident (daytime somnolence).

- **Total arousal index (TAI):** It is the total number of arousal per hour. The arousal is detected clinical or by EEG.
- **Respiratory disturbance index (RDI):** It is the sum of AHI and TAI.

• **Oxygen desaturation index (ODI):** is the number of times the patient has a decrease in oxygen saturation greater than 4% per hour.

Treatment of OSAHS:

1- CPAP Mask: but not all patients tolerate the mask. **The level of positive pressure** required to sustain the patency of the patient's upper airway during sleep **must be determined in a sleep laboratory.**
2- Oral Appliances: to move the tongue anteriorly, together with nocturnal O_2 administration.
3- Surgery: • Uvulopalato-pharyngoplasty (laser-assisted).
• Genio-glossus advancement.
• Maxillo-mandibular advancement.
• Tracheostomy.

Anesthetic Management of OSAHS:

In addition to **the above anesthetic management of obese patients**, the following considerations should be taken:
1- The perioperative risk should be determined as mentioned below.
2- In emergency surgery with no time for assessment, suspected patients should be treated as if they had severe OSA.
3- OSA patients should be considered as inpatients because of:
a- Patient factors:
• There is increased sensitivity to opioids and sedatives, which cause decreased tidal volume, relaxation of pharyngeal muscles, and decreased arousal.
• Respiratory problems as decreased FRC and hypoxia.
• Cardiovascular problems as hypertension and biventricular hypertrophy.
b- Hospital factors:
• Specialized airway equipment are needed.
• Respiratory equipment e.g., CPAP or ventilators are needed.
• Monitoring equipment e.g., SpO_2, chest x-ray, 12-lead ECG, arterial blood gases, and invasive monitors are needed.
• Availability of skilled personnel is important.

Some OSA patients are **exceptionally** considered as **outpatients** as those:
• With mild OSA.
• Who will have local or regional anesthesia with no or minimal sedation.
• Who will have several to 23-hour postoperative post-anesthetic care unit (PACU) observation period.
• Who will be on oral medications at the time of discharge.

4- Special precautions during recovery and extubation should be taken (see above).
5- Special precautions in the postoperative period should be taken (see above).

Determination of Perioperative Risk: It depends on calculating the severity of OSA, invasiveness of anesthesia and/or surgery, and postoperative opioid requirements as follows:

a) Severity of OSA: Classifications (Grades and Scores) of OSA

	Mild OSA (scored as 1)	Moderate OSA (scored as 2)	Severe OSA (scored as 3)
Clinical Picture	Besides the complications of obesity discussed above.		
	• **Obese**. • **Snore most of the time they sleep** (but not necessarily all the time because the snoring may be position-dependent i.e., positive while supine and negative while in the lateral or prone positions). • The patient **has not has definitive observed apneas or arousals during sleep.** • The patients **falls asleep** during **some of the quiet times** during each day.	It is **in between** the two extremes.	• **Morbidly obese.** • **Snore virtually all the time they sleep.** • The patient has **definite observed apnea and frequent arousals,** but occasionally has apnea that is unaccompanied by arousals and therefore, becomes cyanotic (creating panic in observers) • The patient **falls asleep** during **most/many of the quiet times** during the day.
Sleep Study The AHI	6-20	21-40	> 40
The ODI	60-69% of the time the patient is desaturated	70-79%	80-89%

b) Severity of Invasiveness of Anesthesia and/or Surgery:

	Grade/Score 0 (Minimal Invasiveness)	Grade/Score 1 (Mild Invasiveness)	Grade/Score 2 (Moderate Invasiveness)	Grade/Score 3 (Severe Invasiveness)
Surgery performed	Superficial	Superficial	Superficial	Either major or airway surgery
Anesthesia used	**Local** anesthesia or peripheral nerve block with **no sedation**	**Local** anesthesia or peripheral nerve block but with **moderate sedation**	**General** anesthesia	**General** anesthesia

c) Postoperative Opioid Requirements (POR)

- Grade/score 0: no POR.
- Grade /score 1 (mild): a low dose oral POR.
- Grade/score 2 (moderate): moderate-dose oral POR.
- Grade/score 3 (severe): high-dose oral or parenteral or neuraxial POR.

Calculating the Perioperative Risk:

Perioperative risk = severity of OSA (1, 2, or 3) + either severity of invasiveness of anesthesia and/or surgery (0, 1, 2, or 3) or postoperative opioid dose (0, 1, 2, or 3) which is greater.

For example:

- Moderate OSA 2, invasiveness moderate 2, POR 1; therefore, the perioperative risk is 2 + 2 = 4.
- Mild OSA 1, invasiveness 1, POR 3; therefore, the perioperative risk is 1 + 3 = 4.

The American Society of Anesthesiologists OSA Guidelines defines:

- **Increased risk:** with a risk score of **4**.
- **Significantly increased risk:** with a risk score of **≥ 5**.

The American Society of Anesthesiology made the following recommendations and guidelines according to the perioperative risk determined:

a) Increased perioperative risk OSA (risk score of 4):

- Any facility in which the surgery is to be performed should have:
  - Emergency difficult airway equipment.
  - Respiratory care equipment (nebulizers, CPAP machines, ventilators).
  - Portable chest x-ray capability.
  - ECG capability.
  - The ability to measure arterial blood gases, electrolytes, hemoglobin (or hematocrit).
  - A transfer arrangement to an inpatient facility.
- Airway surgery (e.g., uvulopalatopharyngoplasty) in adults, tonsillectomy in children less than 3 years of age, and upper abdominal laparoscopy in adults should not be performed on an outpatient basis.

b) Significantly increased perioperative risk OSA (risk score of ≥ 5):

These patients are generally not good candidates for surgery in a freestanding facility (non-hospital).

Childhood Obstructive Sleep Apnea (COSA)

COSA ranges from snoring and upper airway resistance syndrome, to the fully expressed syndrome.

Causes: Mainly peripheral causes due to nocturnal airway blockage from nasal pathophysiology, hypertrophic tonsils and adenoids, or craniofacial dysostosis.

Clinical Picture:

- It occurs in children of all age groups (about 2% of all children), but more commonly in children 3-7 years of age.
- Unlike adult OSA, snoring is usually more continuous in COSA and there is no sex predilection, and surgery (commonly adenotonsillectomy, rarely uvulopalatopharyngoplasty) is curative.
- Rare daytime sleepiness.
- Besides the clinical picture of OSA such as obesity and snoring, there is failure to thrive (from poor food intake resulting from tonsillar hypertrophy), speech disorders, and decreased body size (due to decreased growth hormone release during disturbed rapid eye movement sleep).
- Frequent behavioral disturbances (e.g., attention deficit/hyperactivity disorder).
- Sleep apnea may be central apnea, obstructive apnea or mixed.

Investigations:

If COSA is suspected, a full blood count (to detect polycythemia), pulse oximetry, and ECG (to detect signs of cor pulmonale) should be performed.

Malnutrition

Causes: persistent anorexia, dysphagia (e.g., due to gastrointestinal cancer), vomiting...etc.

Anesthetic Problems and Considerations:

All the following items are decreased.

1- Fluid depletion: Hypovolemia and dehydration occur resulting in:

- decreased glomerular filtration rate up to irreversible acute tubular necrosis.
- orthostatic hypotension, and
- impairment of liver function tests.

2- Electrolyte imbalance: e.g., **hypokalemia** due to repeated vomiting, which may cause sudden death due to increased incidence of ventricular arrhythmias.

3- Hypoproteinemia: Serum albumin decreases < 2.5-3 g/dL; therefore, human albumin infusions are needed.

4- Vitamins and minerals deficiency: such as iron deficiency resulting in **hypochromic anemia, vitamin deficiencies** (see later); therefore, multivitamin preparations should be given.

5- Depressed immune system: There is an increased risk of **infections** as chest infections, wound infection…etc.

6- Delayed wound healing: resulting in wound dehiscence.

7- Delayed gastric emptying: increasing the risk of aspiration.

8- Decreased bone density and osteoporosis: with increased possibility of fracture during positioning.

9- Decreased muscle strength: especially of respiratory muscles resulting in pulmonary dysfunction.

10- Depressed cardiovascular system: decreased venous return causing decreased cardiac output (with bradycardia and hypotension) due to:

- Decreased contractility.
- Cardiomyopathy (due to starvation).
- Dehydration, hypovolemia, and reduced blood volume.
- Decreased free fat body mass.
- Decreased core temperature.
- Decreased O_2 consumption (due to decreased metabolism).
- Decreased T_3 level.

11- Decreased body temperature: that may affect other functions in the body such as coagulation.

12- Decreased blood components: anemia, neutropenia, and thrombocytopenia.

13- Treatment:

- Nutritional support can be applied either **preoperatively or postoperatively**. **Preoperative nutritional support for 7 days before surgery** decreases postoperative complications especially in patients with gastrointestinal cancer and elderly patients undergoing surgery for hip fracture.
- Nutritional support can be provided either **enterally** (via a nasogastric or gastrostomy tube feeding) or **parenterally** (via i.v. infusion) according to the patient's condition. Parenteral and total parenteral nutrition (indications, components, methods of administration, and complications) are discussed in more details in chapter "Intensive Care".

Vitamin Deficiencies

Vitamin deficiencies are usually associated with severely malnourished patients. They are diagnosed by decreased vitamin levels in urine or plasma. Some of the vitamin deficiencies are discussed in the following table:

Vitamin Deficiency	Causes of Deficiency	Clinical Picture
Vitamin A	Dietary deficiency as leafy vegetables and animal liver, or malabsorption.	**Ophthalmic manifestations** as loss of night vision, conjunctival drying, corneal destruction and **anemia**.
Vitamin B_1 (Thiamine)	Chronic alcoholism	**Beriberi disease;** characterized by hyperdynamic circulation, polyneuropathy, lactic acidosis, **Wernicke's encephalopathy** (impaired sensory perception), and bleeding tendency.

Vitamin B_2 (Riboflavin)	Dietary deficiency	**Ariboflavinosis;** characterized by cheilosis (cracks in lips), photosensitivity, glossitis (inflammation of the tongue), angular stomatitis, seborrheic dermatitis, pharyngitis, and pharyngeal edema.
Vitamin B_3 (Niacin)	Carcinoid tumor	**Pellagra;** characterized by aggression, irritability, mental confusion, dermatitis, insomnia, weakness, and diarrhea.
Vitamin B_5 (Pantothenic acid)	Dietary deficiency as meats, outer layers of whole grains, vegetables, yeast, and egg yolks.	**Acne and nonspecific picture** as paresthesia, depression, gut upset, and cramps.
Vitamin B_6 (Pyridoxine)	Chronic alcoholism and isoniazid	**Microcytic anemia, dermatitis, hypertension, neurological manifestations** as depression, convulsions, neuropathy, and confusion and elevated homocysteine level.
Vitamin B_7 (Biotin)	Dietary deficiency as egg yolk, liver, and some vegetables. Egg white contains the protein avidin, which strongly binds the biotin. Egg cooking deactivates avidin while biotin remains intact.	**Mental changes** (depression, paresthesia, hallucination) and **dermatitis.**
Vitamin B_8 (Inositol)	Dietary deficiency as meats, liver, milk, and eggs.	Very rarely produces clinical picture.
Vitamin B_9 (Folate or Folic Acid)	Chronic alcoholism, sulfasalazine, triamterene.	**Megaloblastic macrocytic anemia**, atrophic glossitis, depression, and increased level of homocysteine. Deficiency in pregnant women can lead to birth defects. Supplementation is often recommended during pregnancy.
Vitamin B_{10} (Factor R)	Dietary deficiency	Very rarely produces clinical picture as slow growth
Vitamin B_{12} (Cyanocobolamine)	Gastric atrophy (pernicious anemia), terminal ileal disease, strict vegetarian people.	Megaloblastic macrocytic anemia, peripheral neuropathy, cognitive dysfunction, and elevated homocysteine.
Vitamin C (Ascorbic Acid)	Smoking and chronic alcoholism	**Scurvy;** characterized by capillary fragility, petechial hemorrhage, joint hemorrhage, poor wound healing, loosened teeth and gangrenous alveolar margins.
Vitamin D	Dietary deficiency as fish e.g., salmon, whole egg, liver, mushrooms (are the only vegetable source of vitamin D). Lack of ultraviolet light or sunlight exposure.	**Rickets (in children);** characterized by thoracic kyphosis (restrictive lung disease). **Osteomalacia (in adults)** low serum calcium, and phosphate.
Vitamin E	Fat malabsorption	Peripheral neuropathy, ataxia, muscle atrophy, and retinopathy.
Vitamin K	Formed by intestinal bacteria that are eliminated by prolonged antibiotic therapy or fat malabsorption. Other causes are discussed in the chapter of "Blood Diseases".	Bleeding tendency.

N.B.: In older literature, adenine was sometimes called Vitamin B_4. It is no longer considered a true vitamin or a part of the vitamin B complex. Also, vitamin B_{11} is no longer considered as a true vitamin as it has been determined later to be a mixture of substances.

Eating Disorders

These disorders are characterized by serious disturbances in eating (restriction or bingeing) and excessive concerns about body weight. Eating disorders typically occur in **adolescent girls or young women**, but sometimes affect boys and young men.

These disorders are usually accompanied by depression, anxiety disorders, and personality changes.

These disorders are usually treated with **tricyclic antidepressants** and selective serotonin reuptake inhibitors (fluoxetine).

1- Anorexia Nervosa

It is a relatively rare psychiatric disorder due to **self-imposed dietary restriction with purging** (inducing self-vomiting and usually associated with excessive use of diuretics and laxatives) to decrease body weight. The patient usually denies his condition.

Anesthetic Considerations and Clinical Picture:

- **Body mass index < 17.5 kg/m².**
- **Fear of weight gain** and inaccurate perception of body shape and weight as the patient feels that his or her body is still obese despite of the dramatic weight loss.
- **Amenorrhea.**
- **The clinical picture of malnutrition** is present (as above).
- **ECG changes** such as sinus bradycardia, low QRS amplitude, nonspecific ST-T wave changes, U wave, prolonged QT interval, and heart block.

2- Bulimia Nervosa

- It is a chronic disease, characterized by **episodes of binge eating** (a sense of loss of control over eating), usually twice weekly for 3 months, **purging, excessive exercise, and fasting** with relapses and remissions. Binges are most often triggered by a negative emotional experience.
- There are signs of **dehydration**, hypertrophy of salivary glands (with **elevated serum amylase** from the salivary glands), and **metabolic alkalosis** (due to purging).
- Psycho-pharmacological treatment such as tricyclic antidepressants and selective serotonin reuptake inhibitors (fluoxetine) are tried.

3- Binge-Eating Disorders

- It is a chronic disease **with binge episodes**, resembles bulimia nervosa, but in contrast to patients with bulimia nervosa, these individuals **do not purge** and periods of dietary restriction are less obvious. The patients are usually **morbidly obese**.
- The binge episode is characterized by:
  - recurrence (2 days/week for 6 months),
  - eating rapidly, until uncomfortably full,
  - eating when not hungry, and
  - eating alone, with feeling guilty after a binge.

Inborn Errors of Metabolism

They are a group of diseases that are characterized by congenital defects in the metabolism. They include:

- Porphyrias.
- Gout.
- Lesch-Nyhan syndrome
- Disorders of carbohydrate metabolism
- Disorders of amino acid metabolism.

Porphyrias

Porphyrias are a group of inborn errors of metabolism characterized by overproduction of porphyrins and their precursors due to a defect in any of the enzymes responsible for porphyrin metabolism resulting in accumulation of the preceding intermediaries.

Heme is the most important porphyrin in human body. It is bound to proteins to form hemoproteins such as hemoglobin and cytochromes (P-450 isoenzymes), which are important for drug metabolism). Production of the heme is controlled by the activity of **D-amino-levulinic acid (DALA) synthetase** enzyme.

Types of Porphyrias:

There are different types of porphyrias according to the site of enzymatic defects. Only acute forms of porphyria are relevant to the management of anesthesia, as they are the only forms of porphyria that may result in life-threatening reactions in response to certain drugs. Porphyrias include:

a- Acute:

- Acute intermittent porphyria.
- Variegate porphyria.
- Hereditary porphyria.
- Plumboporphyria.

b- Non-acute:

- Porphyria cutanea tarde.
- Erythropoietic porphyria (uroporphyria or protoporphyria)

Acute Porphyrias:

They are **autosomal dominant** inherited diseases characterized by acute attacks, which occur spontaneously or are precipitated by events that decrease heme concentrations, thus **increasing the activity of DALA synthetase** (as a feedback control trying to increase heme production to its previous level). The effect of precipitating factors only affects the acute porphyrias and not the other non-acute forms.

Precipitating Factors: include enzyme-inducing drugs (the most important inducing factor) (see later), and physiologic hormonal fluctuations such as these that accompany menstruation, fasting (such as before elective surgery), dehydration, stress (such as that associated with anesthesia and surgery), and infection.

	Safely used drugs	**Drugs used with care** as no data is present or probably safe	**Unsafe drugs, which** should be avoided
1- I.v. agents	Propofol	Ketamine	Barbiturate (thiopental, methohexital), etomidate
2- Volatile agents	N_2O, cyclopropane, diethyl ether	Halothane, isoflurane, sevoflurane, desflurane	Enflurane
3- Muscle relaxants	Curare, suxamethonium, pancuronium	Atracurium, cisatracurium, vecuronium, rocuronium, mivacurium	alcuronium
4- Neuromuscular blockade reversal	Atropine, glycopyrrolate, neostigmine		
5- Local anesthetics	Lidocaine, bupivacaine, procaine, amethocaine, tetracaine	Prilocaine, ropivacaine	Mepivacaine
6- Analgesics	Paracetamol, aspirin	Ketorolac, phenacetin	
7- Opioids	Morphine, codeine, meperidine, fentanyl, sufentanil, buprenorphine, naloxone	Alfentanil	Pentazocine
8- Anxiolytics	Temazepam, midazolam, lorazepam, droperidol, phenothiazines	diazepam, triazolam, oxazepam	Other benzodiazepines
9- Anti-arrhythmics	Procainamide, β blockers	Lignocaine, mexiletine, bretyllium, disopyramide	Verapamil, phenytoin, nifedipine, diltiazem
10- Cardiovascular drugs	Adrenaline, α-agonists, β agonists, β- antagonists, phentolamine	Na nitroprusside, diltiazem, nifedipine	Hydralazine, phenoxybenzamine
11- Bronchodilators	Corticosteroids, salbutamol	Hexaprenaline	Aminophylline
12- Gastric drugs	Metoclopramide, domperidone	Cimetidine, ranitidine, ondansetron	

The above table is only a guide for physicians because some of the above drugs are based on animal or cell culture experiments and may not be true in human.

Clinical Picture:

Acute porphyrias are characterized by **acute attacks** of signs and symptoms **with complete and prolonged remissions in between the attacks**. Many individuals with porphyria never develop symptoms **(i.e., silent or latent porphyria)** may experience their first symptoms in response to inadvertent administration of triggering drugs during the perioperative period. There may be:

- **Central nervous manifestations:**
  - Autonomic neuropathy as fever and pain.
  - Neuro-psychiatric disturbances.
  - Motor and sensory peripheral neuropathy with skeletal muscle weakness that may progress to quadriparesis, bulbar palsy (with possibility of aspiration), and respiratory failure.
  - Cranial nerve palsies.
  - Seizures.
- **Gastrointestinal manifestations** as acute abdominal pain (which may mimic acute appendicitis, acute cholecystitis, renal colic, but clinical examination of the abdomen is typically normal), vomiting, diarrhea, dehydration, electrolyte disturbances (sodium, potassium, and magnesium).
- **Cardiovascular manifestations** as tachycardia, hypertension, and less commonly hypotension.

	Defective Enzyme	Clinical Picture
Acute Intermittent Porphyria	Propho-bilinogen deaminase due to a defect in a gene on chromosome 11.	It is the most common type. It is the most life threatening porphyria. It is characterized by severe hypertension, renal dysfunction, central and peripheral nervous dysfunction.
Variegate Porphyria	Proto-porphyrinogen oxidase due to a defect in a gene on chromosome 1.	It is characterized by neurotoxicity, cutaneous photosensitivity.
Hereditary Copor-prophyria	Copor-porphyrinogen due to a defect in chromosome 9.	It is less severe.
Porphyria Cutanea Tarda	Uro-prophyrinogen decarboxylase	It is non-acute porphyria, characterized by photosensitivity and hepatic dysfunction. Drugs, which precipitate acute porphyrias, do not provoke an attack of porphyria cutanea tarda. Anesthesia is not a hazard in affected patients, although the choice of drugs should take into consideration the likely presence of co-existing liver disease.

Treatment of Porphyric Crisis:

1- Removal of any known triggering factors.

2- Specific therapy:

- Hematin 3-4 mg/kg i.v. over 20 minutes. It supplements the intracellular pool of heme and thus suppresses DALA synthetase activity. It may produce renal failure, coagulopathy, and thrombophlebitis.
- Heme arginate is more stable and without side effects.
- Somatostatin decreases the rate of formation of DALA synthetase.
- Plasmapheresis may be used.

3- Symptomatic treatment:

- Sedatives, analgesics, and antiemetics (from the above table).
- β-blockers are used to control tachycardia and systemic hypertension.
- Seizures are controlled by benzodiazepines (not by traditional anticonvulsants as they are regarded as unsafe drugs).
- Correction of electrolyte disturbances.

Anesthetic Management:

General Considerations:

- Precipitating unsafe drugs should be avoided, while suspicious drugs are used when only their benefits are apparent.
- Short-acting drugs are presumed to be safe because their rapid elimination limits exposure time for enzyme induction to occur.
- Single exposure to potent inducers is tolerated, but not in acute attack.
- Exposure to multiple potential agents is more dangerous than any new single agent.

Preoperative Management:

- Careful history should be taken including **family history**.
- **Preoperative assessment** of cardiovascular, respiratory, and central nervous system is mandatory.
- **Preoperative investigations** include:
  - **Urinary** DALA, porphyrins, and porphobilinogen.
  - **Fecal** porphyrins.
- **Preoperative fasting** should be **minimized** as it may induce an attack, but if prolonged fasting is unavoidable, glucose-saline infusion during the preoperative period may be indicted.
- Premedications: Sedatives and aspiration prophylactic drugs are chosen as above table.

Intraoperative Management:

- **Regional anesthesia** has no absolute contraindications with acute porphyrias but preoperative neurological assessment is essential with close hemodynamic monitoring due to autonomic instability.
- **Propofol and ketamine** can be used safely for induction. Repeated boluses or continuous infusions of propofol can result in different responses.
- **Cardiopulmonary bypass:** Theoretically, cardiopulmonary bypass is a potential risk for patients with porphyria due to presence of stresses such as hypothermia, pump-induced hemolysis, blood loss and its consequent increase in heme demand by the bone marrow, and the large number of drugs administered could increase the risk of developing a porphyric crisis. Nevertheless, **clinical experience does not support increased incidence of porphyric crisis** in those patients when undergoing cardiopulmonary bypass.

Postoperative Management:

- Postoperative ventilation may be required during an acute prophyric crisis.

Gout

It is a disorder of Purine metabolism.

Cause:

a- Primary gout is due to an inherited metabolic defect that leads to overproduction of uric acid.

b- Secondary gout is hyperuricemia due to an identifiable cause, such as increased protein intake, chemotherapeutic drugs used to treat leukemia, leading to the rapid lysis of purine-containing cells.

Anesthetic Considerations (and Clinical Picture):

- **Recurrent attacks of acute arthritis** due to deposition of urate crystals in joints with inflammation of the joint. The most common joint affected is the first metatarsophalangeal joint. **Affection of temporomandibular joint** may cause **difficult intubation**.
- **Renal impairment** (due to deposition of urate in the kidney); therefore, **prehydration with sodium bicarbonate** (to alkalinize the urine) is used to facilitate excretion of uric acid. **Lactated Ringer's solution** may be beneficial because lactate can decrease renal tubular secretion of uric acid (although unproven clinically). **Renal function tests** should be performed.
- **Systemic hypertension, ischemic heart disease, and diabetes mellitus** are common association.
- Treatment:
  - Probenecid *(Benuryl, Benemid, Probalan)*: It is a uricosuric drug, which increases urate excretion.
  - Allopurinol (*Zyloprim*): It inhibits conversion of purines to uric acid by xanthine oxidase.
  - Colchicine (Colchicine, Colcrys): it has no effect on purine metabolism, but relieves joint pain by modifying leukocyte migration and phagocytosis. It may cause vomiting, diarrhea, agranulocytosis, and hepatorenal dysfunction.

Lesch-Nyhan Syndrome

It is an inherited defect in purine metabolism due to a defect in hypoxanthine-guanine phosphoribosyl transferase. This leads to excess purine production and increased uric acid levels. It occurs in men.

It is characterized by mental retardation, seizures, dysphagia, vomiting, malnutrition, and renal impairment up to failure.

Disorders of Carbohydrate Metabolism

They are inherited disorders due to a defect in carbohydrate metabolism that are normally involved in the formation of glycogen from glucose. There are many types such as glycogen storage disease, galactosemia, pyruvate dehydrogenase deficiency, and muco-polysaccharidosis.

Glycogen Storage Disease

- **Severe hypoglycemia** is common, which leads to mental retardation; growth retardation, seizures therefore; oral feedings are required every 2-3 hours and exogenous glucose is usually needed.
- **Chronic metabolic acidosis** occurs leading to osteoporosis; therefore, arterial blood gases are needed. **Lactate-containing solutions should be avoided** due to inability of conversion of lactate to glycogen.
- **Hepatomegaly and renal enlargement (with pyelonephritis)** may occur due to accumulation of glycogen in the liver and kidneys.
- **Bleeding tendency**.

Disorders of Amino Acid Metabolism

They are groups of hereditary diseases characterized by defects in amino acid metabolism, such as phenylketonuria (the prototype due to a defect in phenylalanine hydroxylase), homocystinuria, or maple syrup urine disease.

They are characterized by mental retardation, seizures, metabolic acidosis, hepatic failure, thromboembolism, and dermatitis.

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- http://www.newimageweightloss.com
- http://www.whathealth.com
- http://www.sleep-breathing.bc.ca/sleep.html

BLOOD DISEASES

30

- Disorders of red blood cells
  - Physiological considerations
  - Disorders of decreased red blood cell mass (anemias)
  - Disorders of increased red blood cell mass (polycythemia)
- Disorders of coagulation and clotting factors
  - Physiological considerations
  - Hypocoagulability
  - Hypercoagulability
- Disorders of platelets
  - Physiological considerations
  - Disorders of decreased platelet count or function
    - Thrombocytopenia
    - Thrombasthenia
  - Disorders of increased platelet count or function (thrombocythemia)
- Disorders of white blood cells
  - Physiological Considerations
  - Disorders of decreased white blood cell count
  - Disorders of increased white blood cell count
- Hematologic laboratory tests
- Clinical approach of bleeding patients

Blood or hematologic diseases may affect each component of the blood either with increased or decreased production, due to acquired or hereditary causes, which lead to loss of the normal balance in the blood. Understanding of the normal physiology of the blood is very important to allow proper management of the blood diseases. Usually an advice of a hematologist is required either preoperatively or in the intensive care.

Component	Decreased Number or Function	Increased Number or Function
Red Blood Cells (RBCs) or Erythrocytes	Anemia	Polycythemia
Clotting Factors	Hypocoagulability	Hypercoagulability and thrombophilia
Platelets	Thrombocytopenia and thrombasthenia	Thrombocythemia
White Blood Cells (WBCs) or Leukocytes	Neutropenia and Lymphopenia	Leukemia and lymphoma

Disorders of Red Blood Cells

Physiological Considerations

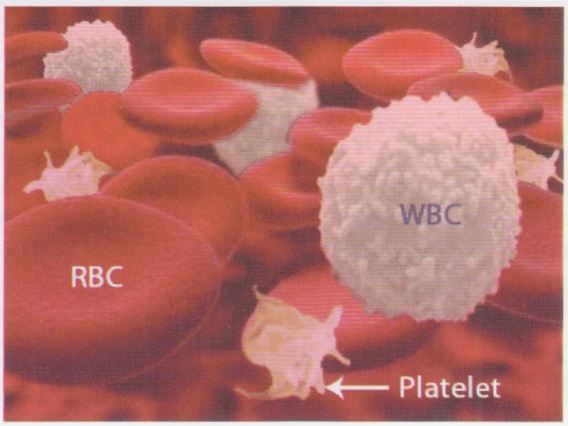
Hemopoiesis (Erythropoiesis)

- **In the fetus**, the main site for hemopoiesis is the **yolk sack until 6 weeks of gestation**. Thereafter **the liver and spleen** are the primary sites **until about 7 months**. Around this stage, **bone marrow** becomes the major site of blood cell production, although the liver and spleen continue to produce red cells in normal individuals until 2 weeks after birth. In extreme situations, the liver may retain hemopoietic potential until much later.
- **In infants, most bones** are involved in hemopoiesis. **By adult life**, this is confined to **the vertebrae, ribs, sternum, sacrum, pelvis, proximal femur, and skull.**
- Hemopoiesis is under control of both humoral and cellular growth factors mainly **erythropoietin** released from the kidney. The main stimulus is hypoxemia.

Red Blood Cells (RBCs):

- The mature RBC at rest takes the shape of a biconcave disc with **a mean diameter of 8 µm**, a thickness of 2 µm, and a volume of 90 fL. The cell is extremely flexible and easily deformable, so it can pass through vessels in the microcirculation whose diameter is less than that of the cell down to 3.5 µm (figure 30-1).

- **The lifespan** of a mature RBC is **approximately 120 days** as it lacks a nucleus and mitochondria and protein metabolic pathway. About 33% of its contents are made of hemoglobin (Hb).
- Intracellular energy requirements are mainly supplied by **glucose metabolism**, which is used to:
  - maintain Hb in a soluble, reduced state,
  - provide appropriate amounts of 2,3-diphosphoglycerate (2,3 DPG), and
  - generate adenosine triphosphate (ATP) to support membrane function and flexibility.



RBC Red blood cell
WBC White blood cell

Figure 30-1: Normal sized red blood cells, white blood cells, and platelets

Hemoglobin (Hb)

- RBCs contain a tetramer of heme groups (4 chains) of Hb, which has the following types:
  - **Adult Hb (Hb A):** formed of 2 α- and 2 β-chains. It represents 96%-97% of total Hb.
  - **Hb A_2:** formed of 2 α- and 2 δ-chains. It represents 2%-2.5% of total Hb.
  - **Fetal Hb (Hb F):** formed of 2 α- and 2 γ-chains. It represents 1.5%-2% of total Hb.
- O_2 binding by one of the heme groups increases the affinity of the other groups to O_2 loading (as Hb is present in tetramers). This interaction is responsible for the **sigmoid shape of the O_2-Hb dissociation curve.**

Disorders of Decreased Red Blood Cell Mass (Anemias)

Definition

Anemia is **decreased Hb concentration** below the lower limit according to the sex and age according to the following table.

Age Groups	Normal Hb Levels
An adult man	12.5 – 18.0 g/dL (hematocrit (Hct) < 40%)
An adult woman	11.5 – 16.5 g/dL (Hct < 36%)
A pregnant woman	Less than 15% of normal values
A 10-12 year old child	11.5 – 14.5 g/dL
A 1 year old child	11.0 – 13.0 g/dL
A 3 months infant	9.5 – 12.5 g/dL (i.e., physiological anemia)
A full term infant	13.5 – 19.5 g/dL

Anemia, like fever, is a sign of disease.

Effects of Anemia

Anemia causes **decreased O_2 content of arterial blood (CaO_2)**, which in turn decreases O_2 delivery to tissues. This initiates **compensatory mechanisms** such as:

1- A rightward shift of the oxy-Hb dissociation curve (which facilitates release of O_2 from Hb to tissues).
2- Increased cardiac output as a reflection of decreased blood viscosity.
3- Release of erythropoietin from the kidney, which subsequently stimulates erythroid precursors in the bone marrow to produce additional RBCs.

Failure of these compensatory mechanisms to maintain tissue oxygenation results in apparent clinical manifestations of anemia such as **easily fatigability, and decreased exercise tolerance**.

Causes

1) Iron Deficiency Anemia:

Type of anemia: It is **microcytic** (smaller than usual) **hypochromic** (paler than usual) **anemia**.

Causes: • Nutritional deficiency,

• Chronic blood loss (e.g., gastrointestinal bleeding, female genital tract bleeding such as heavy menstruation, or regular blood sampling such as in intensive care units).

2) Sideroblastic Anemia:

Type of anemia: It is microcytic anemia

Cause: It is caused by abnormal production of ringed sideroblasts due to **hereditary** or acquired causes such as **lead toxicity** or as a part of **myelodysplastic syndrome**, which may cause acute leukemia. **Sideroblasts** are seen in aspirates of bone marrow; these are atypical nucleated erythrocytes with granules of iron accumulated in peri-nuclear mitochondria.

3) Megaloblastic Anemia:

Type of anemia: It is **macroocytic anemia.** Both vitamins (B_{12} and folic acid) are essential for normal DNA synthesis and complete cell division. High turnover tissues such as bone marrow are the first to become affected when these vitamins are in short supply resulting in lack of ability of cell division, which results in megaloblastic (i.e., with a defect in DNA synthesis) and macrocytic RBCs. The mean red blood cell volume is 110-140 fL (normal =90 fL) with normal reticulocytic count.

Causes:

a- Vitamin B_{12} deficiency: It occurs due to a small intestinal disease or resection, prolonged exposure to N_2O, or atrophy of gastric mucosa (resulting in a decrease in the **intrinsic factor**. It is sometimes called **pernicious anemia**). Other clinical pictures of vitamin B_{12} deficiency are also present such as bilateral peripheral neuropathy (avoid local and regional anesthesia), mental depression, and memory impairment.

b- Folic acid (folate) deficiency: It occurs due to dietary deficiency as during pregnancy and alcoholism (alcohol interferes with folate metabolism). Other clinical pictures of folate deficiency are also present such as peripheral neuropathy, liver dysfunction, hyper-pigmentation, and a smooth tongue.

Other macrocytic non-megaloblastic anemia

They have normal DNA synthesis but with macrocytic cells such as chronic alcoholism, hypothyroidism, and sometimes in chronic liver diseases.

4) Anemia of Chronic Disorders:

Type of anemia: It is **normocytic anemia (Sometimes microcytic anemia).**

Causes: It is of an unknown mechanism. It is associated with:

• Chronic inflammation such as chronic infections (human immunodeficiency virus) or connective tissue disorders.
• Malignancies.
• Uremia.
• Liver diseases especially alcoholic cirrhosis.
• Endocrine diseases such as diabetes mellitus.

5) Physiological Anemia of Pregnancy:

Type of anemia: It is **normocytic anemia.**

Causes: **Increased blood volume** 40% to reach 85-90 mL/kg at term. This occurs due to increased plasma volume 45% and increased red blood cell volume 20%. This causes a dilutional effect, which is **maximal at 32 weeks of pregnancy**. This results in **physiological anemia of pregnancy** (i.e., decreased hemoglobin to 12 g% and hematocrit to 36% "about 15 % of the normal values").

This allows the pregnant woman to control blood loss during vaginal delivery (400-500 mL) and cesarean section (800-1000 mL).

6) Aplastic Anemia:

Type of anemia: It is **normocytic anemia.** There is decreased RBCs resulting in anemia,
decreased WBCs resulting in infection, and
decreased platelets resulting in thrombocytopenia.

Causes: depressed bone marrow occurs due to different causes.

a- Acquired: • Drugs: ▫ Anti-neoplastics (chemotherapy).
▫ Antibiotics (chloramphenicol, penicillin, cephalosporins, sulfonamides).
▫ Antidepressants (lithium, tricyclics).

- Antiepileptics (dilantin, carbamazepine, valproic acid, phenobarbitone).
- Anti-inflammatory drugs (phenylbutazone, non-steroidals, salicylates, gold salts).
- Anti-arrhythmics (lidocaine, quinidine, procainamide).
- Antithyroid drugs (propylthiouracil).
- Antihypertensives (captopril).
- Antiuricemics (allopurinol, colchicine).
- Antimalarials (quinacrine, chlorquine).
- Anti-diabetics (tolbutamide).
- Anti-anxiety drugs (prochlorperazine, meprobamate).
- Anti-platelet drugs (ticlopidine).
- Diuretics (thiazides, furosemide).

• Radiotherapy.
• Viral infections such as viral hepatitis and human immunodeficiency virus.
• Malignancy such as leukemia and bone secondaries invading bone marrow (breast, lung, or prostate).

b- Hereditary: • **Fanconi syndrome:** it is a congenital (autosomal recessive) aplastic anemia.
• Diamond-Blackfan syndrome: it is congenital pure erythrocyte aplastic anemia.

7) Hemolytic Anemia:

Types of anemia: It is **normocytic anemia** except thalassemia and Hb C anemia which are microcytic.
Causes: There is shortening of RBC lifespan below the expected 120 days.

a- Acquired:

1- Extrinsic Factors:

• **Splenomegaly and hypersplenism.**
• **Immuno-hemolytic anemia:** due to presence of antibodies against RBCs. Antibodies are either:
- **Warm antibodies** as with leukemia, lymphomas, systemic lupus erythematosis, drugs (α-methyldopa, penicillin, quinidine), or idiopathic.
- **Cold antibody** as with mycoplasma infection, infectious mononucleosis, or paroxysmal cold hemoglobinuria.

• **Mechanical trauma:** as cardiac valve prosthesis.
• **Microangiopathic hemolytic Anemia** such as hemolytic uremic syndrome.
• **Direct toxic effect** as with malaria and clostridial infection.

2- Membrane Abnormalities:

• **Spur cell anemia:** in Laennec's cirrhosis.
• **Paroxysmal nocturnal hemoglobinuria**: It is associated with increased risk of venous thrombosis and bone marrow aplasia. It is due to a defect in a membrane protein called glycosylphosphatidyl glycan.

b- Hereditary:

1- Intrinsic Factors:

• **Enzyme defects:**
- **Glucose-6-phosphate dehydrogenase (G6PD) deficiency** (see later).
- **Pyruvate kinase deficiency:** It is the most common erythrocyte enzyme defect causing congenital hemolytic anemia. It is due to autosomal recessive inheritance. Although it is more common than G6PD deficiency anemia, it is usually not apparent clinically, but sometimes a mild up to severe hemolytic anemia occurs.

In both G6PD deficiency and pyruvate kinase deficiency, the RBC membrane becomes highly permeable to K^+, resulting in RBC rupture.

• **Hemoglobinopathies:**
- **Sickle cell syndrome** (see later).
- **Met- and sulf-hemoglobinuria** (see later).

• **Impaired production of normal globin chains:**
- **Thalassemia** (see later).

2- Membrane Abnormalities:

• **Hereditary Spherocytosis:** it is autosomal dominant disorder due to a protein defect in the RBC membrane (called **spectrin and ankyrin**), which allows Na^+ influx resulting in increased osmotic pressure intracellularly; therefore, water enters inside the RBCs resulting in their swollen (i.e. spherocytic shape) shape. The cells cannot be compressed and become easily ruptured during passage

in microcirculation e.g., via the spleen, causing decreased lifespan with mild to severe hemolytic anemia.

- **Hereditary Elliptocytosis:** It is an autosomal dominant disorder due to a protein defect in the RBC membrane (called **spectrin and glycophorin**), which results in elliptical cells. It is similar to hereditary spherocytosis but less severe.
- **Acanthocytosis:** It is due to a lipoprotein-B defect in RBC membrane resulting in accumulation of cholesterol on the outer surface of RBCs, giving a spiculated appearance that signals macrophages of reticulo-endothelial system to cull RBCs from circulation. This causes hemolysis and hemolytic anemia.

Clinical Picture of Anemia

The severity of clinical picture often reflects the speed of onset more than the degree of anemia because there is less time for adaptation and for effects of compensatory mechanisms.

- **Symptoms of the cause** such as neuritis of vitamin B_{12} deficiency or heavy menstruation in iron deficiency anemia.
- **Fatigue, dyspnea, palpitations, headache, and angina.**
- **Clinical picture of hemolytic anemia** such as **jaundice, pigmented gallstones, and splenomegaly,** in addition to specific clinical picture as crisis in sickle cell anemia.

Investigations of Anemia

Actually, there is no single laboratory value that defines anemia.

1- Hemoglobin (Hb) level: It is decreased.

2- Hematocrit (Hct):

- The Hct may be unchanged despite acute blood loss, whereas in parturients, decreased Hct values reflect increases in plasma volume and not anemia.
- Decreased Hct that exceeds 1% every 24 hours can only be explained by acute blood loss or intravascular hemolysis.

3- Mean corpuscular volume (MCV): normal = 80-100 fL.

- Microcytic hypochromic anemia: with a MCV of < 80 fL as:
  - Iron deficiency anemia.
  - Anemia of chronic diseases (but usually normocytic anemia).
  - Thalassemia.
  - Hb C syndrome.
  - Sideroblastic anemia.
- Macrocytic anemia: with a MCV of >100 fL as:
  - Vitamin B_{12} and folate deficiency.
  - With some drugs as methotrexate or zidovudine which inhibit DNA replication and cell division.
- Normocytic anemia: with a MCV of 80-100 fL as:
  - Physiological anemia of pregnancy.
  - Anemia of chronic diseases.
  - Acute blood loss
  - Aplastic anemia
  - Hemolytic anemia (except thalassemia and Hb C anemia).

4- Reticulocytic count: normal 1%.

- Increased levels 10-20% indicate hemolytic anemia due to increased RBC production.

5- Other tests that can help to reach the diagnosis such as increased unconjugated bilirubin and hemoglobinuria (indicate RBC breakdown in hemolytic anemia), serum ferritin, B_{12} and folate levels, erythrocyte sedimentation rate (ESR), liver and renal function tests, and even bone marrow aspiration if needed.

Anesthetic Management of an Anemic Patient

The following anesthetic management can be applied generally for all types of anemia.

1- The **type and cause of anemia** should be detected and **avoided, if possible**, pre-, intra-, and postoperatively.

2- The **degree of anemia** should be assessed and **managed. Hb 10 g/dL** is considered the minimum allowed Hb level for elective surgery.

- Iron deficiency anemia is usually treated by the following:
  - **Oral iron is given for at least 1 year** after **stoppage of the source of bleeding** because iron stores are replenished slowly. It is not suitable for elective surgery.

- **Recombinant human erythropoietin** is usually used before elective surgery.
- **Blood transfusion** is usually indicated before emergency surgery.

• **Blood transfusion trigger point:**

The decision to administer RBCs during the perioperative period (pre-, intra-, or postoperative) is influenced by the risks of anemia (decreased O_2-carrying capacity) and the risks of blood transfusion (hemolytic and non-hemolytic reactions and transmissible diseases). Strategies of blood transfusion trigger point (liberal and restrictive) and determination of the trigger point are discussed in the chapter of "Fluid and Electrolyte Disturbances".

3- **Avoid** factors that interfere with O_2 delivery to tissues such as:

• **Avoiding drug-induced decreased cardiac output.**

• **Avoiding factors, which cause left shift of the O_2-Hb dissociation curve** e.g., respiratory alkalosis due to hyperventilation and hypothermia.

4- **Measures decreasing blood loss (and blood transfusion)** discussed in the chapter of "Fluid and Electrolyte Disturbances".

Q: Discuss the anesthetic management of hemoglobinopathies?

Q: Discuss the anesthetic management of hemolytic Anemia?

Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency

• It is an **X-linked** disorder (affects males).

• RBCs contain higher levels of glutathione reductase than any other cell in the body as this antioxidant protects RBCs normally from the toxicity of the very high level of O_2 it is transporting. The sulf-hydryl groups on Hb are protected by reduced glutathione, the latter is regenerated by reduced nicotinamide adenine dinucleotide phosphate (NADPH), which is regenerated from glucose metabolism in the hexose mono-phosphate shunt. G6PD enzyme is critical in this pathway; so, its deficiency decreases NADPH, which decreases reduced glutathione. This causes oxidation and phosphorylation of Hb in RBCs (seen as Heinz bodies) resulting in hemolysis.

• Hemolysis is induced by:

- Fava beans.
- Bacterial or viral infections.
- Metabolic acidosis.
- Drugs as:
  - Analgesics: phenacetin, acetaminophen, aminosalicylic acid.
  - Antibiotics: nitrofurantoin, nalidixic acid, penicillin, streptomycin, chloramphenicol, isoniazid, and sulfonamides.
  - Anti-malarial drugs.
  - Others as probenecid, quinidine, quinine, vitamin K analogues, methylene blue, nitroprusside, and prilocaine (the last 2 drugs cause met-hemoglobinemia, which cannot be treated by methylene blue. Both drugs should be avoided).

• The clinical picture can be divided into 3 categories; a chronic hemolytic anemia, an acute episodic hemolytic anemia, and no apparent risk of hemolysis.

Thalassemia

It is hereditary hemolytic anemia due to a defect in Hb synthesis. The accumulating unpaired globins aggregate and precipitate, forming inclusion bodies that cause membrane damage to the RBCs and hemolytic anemia. Some of these defective RBCs are destroyed within the bone marrow, resulting in ineffective erythropoiesis and hypochromic microcytic anemia.

It is classified according to the defective chain of Hb into:

a- **Beta-thalassemia**: It is a congenital defect in the synthesis of the β globin chain of Hb A resulting in:

• **β-thalassemia trait (minor):** due to a heterozygous state causing no or a mild clinical picture.

• **β-thalassemia intermedia:** due to a double heterozygous or homozygous state causing a moderate clinical picture.

• **β-thalassemia major (Cooley's anemia):** due to a homozygous state causing a severe clinical picture.

b- **Alpha-thalassemia**: It is a congenital defect in the synthesis of the α globin chain of Hb A resulting in:

• **α-thalassemia trait (Hb H disease):** due to a heterozygous state causing a mild clinical picture.

• **α-thalassemia major:** due to a homozygous state causing a severe clinical picture.

Clinical Picture:

• Hemolytic anemia (usually microcytic hypochromic anemia).

- Hepato-splenomegaly and hypersplenism.
- Skeletal changes due to extra-medullary hemopoiesis resulting in craniofacial deformities, over-growth of the maxilla (with difficult intubation), frontal bossing, and spinal cord compression.
- Hemothorax.
- Liver cirrhosis and cardiac hemochromatosis (resulting in supraventricular tachycardia and congestive heart failure) due to chronic blood transfusion.

Sickle Cell Syndrome

Classification:

a- Sickle cell anemia (SS): with a homogenous gene (Hb S level is >80%) resulting in a severe clinical picture.

b- Sickle cell trait (AS): with a heterogeneous gene (Hb S level is >50%) resulting in no or mild clinical picture.

c- Other types:

- **Sickle cell Hb C anemia (SC):** It is either a homogenous or a heterogeneous gene. It represents 25% of sickle cell syndrome. Two abnormal types of Hb are present; Hb S (see below) and Hb C (in which the glutamic acid in the 6th position of the β chain is replaced by lysine). Hb C causes the RBCs to lose water, resulting in RBC dehydration, which increases the concentration of Hb S resulting in sickling and then hemolytic anemia.
- **Sickle cell thalassemia (S β thalassemia):** It represents 10% of sickle cell syndrome. Two defects are present; Hb S and β-thalassemia. The clinical picture is similar to that of SS (see below).
- **Sickle cell Hb E anemia (SE):** Two abnormal types of Hb are present; Hb S and Hb E (in the latter, there is a single substitution on the β chain).

Pathology of Hb S:

- It is hereditary hemolytic anemia transmitted as **autosomal recessive.** The Hb gene is on **chromosome 11.** In sickle cell Hb (Hb S), **valine is substituted for glutamine at position 6 of the β-chain.**
- Under certain conditions such as hypoxia, acidosis ...etc, **deoxygenation of Hb S** occurs causing polymerization and binding of Hb S together. Therefore, Hb S becomes less soluble and forms **long crystals,** which **distort RBCs** giving them a crescent shape (**sickle shape**). **These RBCs have a much shorter survival of 10-15 days** (compared with 120 days in the normal RBCs) resulting in hemolytic anemia where Hct of 18 – 30% is usually reached (figure 30-2).
- These rigid sickle cells tend to **aggregate** in the capillaries and venules **obstructing** the flow of blood with subsequent **infarctions and pain (crisis).** Also more acidosis and hypoxia occur, resulting in more sickling i.e., a vicious circle occurs.



Figure 30-2: Normal and sickle shaped RBCs

The Sickling Phenomenon depends on:

1- The Percentage of Hb S (in RBCs) and the Presence of Other Hb

- **A higher percentage** of Hb S causes more sickling.
- Presence of **Hb C or E** causes more sickling.

2- O_2 Tension (Hypoxia):

RBCs sickle at a particular level of deoxygenation according to the type of sickle cell syndrome:

- In **SS** (homozygous), sickling occurs at **40-50 mm Hg** PaO_2 i.e., at the physiological venous O_2 tension. Sickling starts at $SaO_2 < 85\%$ and is complete when SaO_2 reaches 38%.
- In **SC**, sickling occurs at **30 mm Hg** PaO_2.
- In **AS** (heterozygous), sickling occurs at **20 mm Hg** PaO_2 (or at $SaO_2 < 40\%$) i.e., at a very low O_2 level.

3- Acidosis:

It causes shift of the O_2-Hb dissociation **curve to the right** (i.e., more O_2 is delivered to the tissues) leaving more deoxygenated Hb in RBCs, which produces more sickling.

Factors Causing Hypoxia and Acidosis:

- Hypothermia (resulting in vasoconstriction)
- Dehydration
- Over-transfusion.

They increase blood viscosity causing stasis.

- Infection.
- Hypotension.

These factors cause hypoxia and acidosis.

Clinical Picture:

Patients are often black Africans, black Americans, Mediterraneans, Arabs, and Indians. Patients are often young as the clinical picture appears after disappearance of Hb F.

1- Clinical picture of hemolytic anemia as **jaundice, pigmented gallstones** (which may cause obstructive jaundice), **and splenomegaly. Hyperdynamic circulation** is common due to the chronic anemia.

2- Crises: They are periodic exaggeration of symptoms precipitated by stress e.g., infection, cold weather, dehydration, anesthesia, emotional stress…etc.

There are 4 types of crises:

a- Hemolytic crisis: It is characterized by sudden severe hemolysis, which results in dyspnea, palpitation, jaundice, dark urine (hemoglobinuria), and even renal failure.

b- Aplastic crisis: Viral infection or folate deficiency may cause bone marrow depression, resulting in acute profound aplastic anemia (Hb can reach 2 – 3 gm/dL). There is a reduction of already elevated reticulocytic count differentiating it from other types of crises.

c- Sequestration crisis: It is characterized by acute massive enlargement of the liver and spleen with pooling and trapping of RBCs. It usually affects young children and necessitates immediate transfusion.

d- Vaso-occlusive (infarctive or thrombotic) crisis: It is the most common type as sickling causes aggregation of RBCs within small vessels, which produces infarctions allover the body. This leads to:

- **Bone and joint** pain, hands and feet infarctions (dactylitis), biconcave (fish mouth) vertebrae and osteomyelitis.
- **Chronic leg ulcers**.
- Early in life, **splenomegaly** may occur; then later on in life, multiple splenic infarctions occur causing **asplenism** with loss of its function, leading to repeated bacterial infections.
- **Priapism** (painful penile erection): It is a medical emergency. It is a potentially disastrous complication that may be treated successfully with **epidural analgesia**.
- **Repeated pulmonary emboli** that cause chest pain, corpulmonale, and even congestive heart failure.
- **Myocardial infarctions.**
- **Hepatic infarctions,** which cause hepatic dysfunction, hepatic abscesses, and fibrosis.
- **Renal infarctions** as renal papillary necrosis, which causes hematuria and renal dysfunction up to renal failure.
- **Cerebral infarctions** and intra-cerebral hemorrhages.
- **Retinal infarctions** and detachment, retinopathy, and vitreous hemorrhage.

3- If associated with thalassemia, skeletal deformities may occur such as over-growth of the maxilla.

4- Acute chest syndrome:

- It occurs in patients with sickle cell disease due to vaso-occlusive crisis, infection, or pulmonary fat embolism (due to bone marrow necrosis).
- It is characterized by fever, cough, pleuritic chest pain, tachycardia, and hypoxemia. Chest x-ray usually shows pulmonary infiltrates and pleural effusion.

5- Repeated blood transfusions increase iron load resulting in **hemochromatosis,** which causes liver cirrhosis and left ventricular dysfunction.

Investigations:

1- Solubility test (Sickledex): a commercially available macroscopic test that detects Hb S by a precipitation reaction (a cloudy suspension) within minutes by using **Na meta-bisulfite** (a reducing agent that consumes O_2 causing sickling). It is a simple test, used as a screening test, but it has many limitations:

- It cannot distinguish sickle trait from disease or distinguish other different types of Hb that may be associated with sickle cell diseases (Hb electrophoresis is needed, see later).
- It is not useful in the newborn period because of the presence of a high proportion of Hb F (70-90%). The test may not be positive before 4 months of age because of continued high levels of fetal Hb.
- It can be falsely negative in young children with Hb SC type.
- It is inaccurate after recent blood transfusion or when the total Hb is less than 7 g/dL.

2- Blood film: is performed to confirm the presence of sickle cells.

3- Hb electrophoresis: is a definitive test, which detects different types of Hb and measures their concentration.

4- Isoelectric focusing and high-performance liquid chromatography fractionation is used for newborn screening.

5- Antenatal diagnosis of sickle cell disease is performed late in the first trimester of pregnancy by **DNA analysis of fetal tissue** obtained by chorionic villous sampling or amniocentesis.

Treatment of Sickle Crises:

1- Bed rest, sedation, and analgesics (intramuscular or epidural opioids).

2- Treatment of precipitating factors such as hypoxia (by O_2), dehydration (by i.v. fluids), acidosis (by i.v. $NaHCO_3$), and infection (by antibiotics).

3- Assessment and correction of the level of zinc and magnesium, which are important for RBC hydration and prevention of sickling.

3- Partial exchange transfusion with RBC containing Hb A to increase Hb A up to 50%-70%, but with keeping Hct at < 35%. Partial exchange transfusion is done either manually or via apheresis.

4- Hydroxy-urea stimulates genes that produce **Hb F** leading to clinical improvement.

5- Hyperbaric Oxygen decreases the rate of sickling and improves tissue oxygenation by direct diffusion only in vivo (not in vitro).

6- Recently, hematopoietic cell transplantation: It needs HLA-identical siblings. It cures the recipient in 90% of cases who becomes free of sickle cell disease for 11 years. Many complications occur such as immunosuppression causing infection, graft rejection, graft versus host disease, and lympho-proliferative disease.

Anesthetic Management:

Patients with **sickle cell trait** show **no risk** with anesthesia, but patients with **sickle cell disease** show **an increased risk** with anesthesia.

Preoperative Management:

1) Preoperative Assessment of the Degree of Anemia:

Anemia is corrected by:

1- Preoperative **packed RBC transfusion** to:

- increase Hb A up to 10 g% (Hct up to 25-30%) in anemic patients disregarding Hb S level especially for emergency and non-emergency low-risk patients. Avoid over-correction (i.e., Hb > 11 g%) as a greater increase in Hb causes hyper-viscosity, which increases sickling.
- suppress endogenous erythropoiesis, so Hb S concentration is reduced.

2- Preoperative **partial exchange transfusion** (it is controversial).

- Value: It is sometimes performed to replace Hb S by Hb A until the concentration of **Hb S becomes < 30-60%** while the concentration of **Hb A becomes > 40-70%** (with a Hct of 30%).
- Indications: It is performed mainly for high-risk patients such as:
  - those with Hb concentration **6-7 g%**.
  - those undergoing **major surgeries** such as major body cavity surgery (minor elective surgeries can be done without exchange transfusion).
  - those with preexisting cardiovascular, neurological, or pulmonary dysfunction.

Other indications for exchange transfusion:

- Acute: ▪ Any type of crisis especially that is painful and protracted. ▪ Acute chest syndrome. ▪ Acute multi-organ failure. ▪ Severe unresponsive priapism. ▪ Stroke.
- Chronic: ▪ Intractable leg ulcers.

- Recurrent acute chest syndrome.
- Recurrent painful syndrome.
- Complicated pregnancy.

Recently, the goals of preoperative transfusion management have changed in recent years. Studies examining the effects of aggressive exchange transfusion strategies aimed at increasing the ratio of normal Hb to sickle Hb, have found no benefit compared to the more conservative goal of achieving a preoperative Hct of 30%. Indeed, the aggressive strategies necessitate significantly more transfusions, and the complications of these transfusions outweight their benefits.

Accordingly, low-risk procedures rarely require any preoperative transfusions, and patients undergoing moderate to high-risk procedures need only to have any preoperative anemia corrected to a target Hct 30%.

2) Preoperative Assessment of the Precipitating Factors and their Management: such as infections (by antibiotics), dehydration (by allowing liberal oral clear fluid intake until 2 hours before surgery)…etc.

3) Preoperative Assessment of the Clinical Picture and Other Organ Affections: such as chest, heart, brain, bone, airway (for possibility of difficult intubation)… etc.

4) Premedications:

Sedatives (and opioids) are better decreased or avoided for fear of hypoxia.

Intraoperative Management:

Aim:

1- **Avoid hypoxia** by: • adequate oxygenation (and increasing the FiO_2 to > 0.5) and
• pulse oximetry and mixed venous O_2 partial pressure monitoring.

2- **Avoid acidosis** by: • hyperventilation (to avoid respiratory acidosis),
• $NaHCO_3$ infusion 0.3 mEq/kg/h (to increase the alkali reserve), and
• arterial blood gases monitoring.

3- **Avoid hypothermia** by: • increasing operating room temperature, warming blanket, warm fluid, and gases, and
• body temperature monitoring.

4- **Avoid dehydration** by: • adequate i.v. volume (avoid overload) and
• central venous pressure and urine output monitoring.

5- **Avoid hypotension** by • maintaining cardiac output and tissue perfusion and
• monitoring of pulmonary capillary pressure and invasive blood pressure.

6- **Avoid stasis** by: • avoiding an occlusive orthopedic tourniquet, if possible, and if used, it should be for a very short time after limb exsanguination. Some authors do not consider the tourniquet a contraindication in sickle cell disease, although the incidence of perioperative complications is increased.
• low molecular weight dextran to decrease blood viscosity and
• avoiding increased Hct of > 30% (i.e., avoid over-transfusion).

Monitoring: Besides the standard monitors, other more sophisticated monitors may be required as above.

Choice of Anesthesia:

No particular anesthetic technique is advantageous than another. The anesthetic technique is much less important than correction of the precipitating factors such as hydration, perfusion, and oxygenation.

a) Regional Anesthesia: (some authors prefer it)

• Epidural and spinal anesthesia can be **used safely**, but they may produce compensatory vasoconstriction (and decreased PaO_2) **in the non-blocked area causing more sickling**.
• **Bier block should be avoided.**

b) General Anesthesia: Care is taken for **suspected difficult intubation.**

Postoperative Management:

The same pre- and intraoperative precautions (as above) should be followed with attention to the following: • **O_2 supplementation** for the 1st 24 hours after anesthesia with O_2 saturation monitoring.
• **Chest physiotherapy.**
• **Good analgesics**: Care is taken for respiratory depression of opioids.
• **Avoidance of shivering** and **hypothermia** (as it may lead to hypoxia).
• Postoperative complications:
  - **Any type of crisis** can occur, which needs close observation.
  - **Acute chest syndrome** may develop typically 2-3 days postoperatively, which should be managed.

Met-Hemoglobinemia

Pathology:

• In met-Hb, the Hb A iron exists in the **ferric (Fe^{+++})** rather than the normal ferrous (Fe^{++}) state. Ferric iron is unable to bind O_2 and shifts the oxy-Hb dissociation **curve to the left** decreasing O_2 delivery to the tissues. Normally, **the met-Hb reductase enzyme** changes met-Hb to Hb A i.e., changes the ferric iron to ferrous iron.

• Normal values of met-Hb = < 1% in the blood.

Causes:

1- Congenital absence of met-Hb reductase enzyme leading to formation of met-Hb.

2- Globin chain mutations favoring formation of met-Hb making a resistance to reduction of the globin chain by the met-Hb reductase enzyme.

3- Toxic exposure to substances that oxidize normal Hb iron at a rate that exceeds the capacity of normal reducing enzyme such as nitrate containing compounds as **nitroglycerin, Na^+ nitroprusside, benzocaine, and prilocaine.**

Clinical Picture:

It differs according to the level of met-Hb in the blood.

• **When met-Hb reaches 15% (i.e., 1.5 g/dL) up to 30%:**
  ▫ **Cyanosis** occurs because the met-Hb has a brownish-blue color that does not change to red color on exposure to O_2. Sometimes it is called **pseudocyanosis**.
  ▫ **A discrepancy between the PaO_2 and SaO_2** is present because there is a **low SaO_2** (O_2 saturation of Hb), but there is a **normal PaO_2** (dissolved O_2 in the plasma). The pulse oximeter will read about 85% regardless of the PaO_2.
  ▫ Still no compromise occurs in tissue oxygenation.

• **When met-Hb is between 30-50%**, patients begin to exhibit symptoms of O_2 deprivation such as **lethargy, dizziness, and headache.**

• **When met-Hb becomes > 50%, coma and death** can ensue.

Treatment:

Methylene blue

Indication: Treatment should be started when the level of met-Hb **exceeds 30%.**

Dose: 1-2 mg/kg (1% solution in saline) i.v. over 5 minutes. It can be repeated every 30-60 minutes, if cyanosis persists.

Action: It transfers electrons from reduced nicotinamide adenine dinucleotide phosphate reductase system (NADPH) to met-Hb.

Side Effects: • Doses > 7 mg/kg total may oxidize Hb back to met-Hb.
• In G6PD deficiency patients, hemolytic anemia may occur; therefore, it is better avoided.

Sulf-Hemoglobinemia

Pathology: It is the formation of sulf-Hb, which cannot carry O_2.

Cause: The same drugs causing met-Hb. The reason why some patients form met-Hb and others form sulf-Hb is unknown.

Clinical Picture: as met-Hb.

Treatment:

No response to methylene blue (in contrast to met-Hb); so, the only means of removing sulf-Hb is by the eventual destruction of the affected RBCs.

Disorders of Increased Red Blood Cell Mass

Polycythemia (Erythrocytosis)

Definition: It is an increased Hct of >55%, which increases blood viscosity.

Causes:

A- Primary: Myelo-proliferative disease (polycythemia vera): It produces **absolute polycythemia**.

It is a stem cell disorder that occurs due to gene mutation, giving rise to proliferation of a clone of hematopoietic precursors. It is treated by regular phlebotomies, myelo-suppressive drugs such as hydroxyurea (used for months until reaching a normal blood picture), and O_2 therapy.

B- Secondary:

1- Erythropoietin-secreting tumors and diseases: They produce **absolute polycythemia**.

For example: • Renal diseases as hydronephrosis, polycystic renal disease, renal cysts, benign and malignant renal tumors.
• Uterine myomas, hepatomas, and cerebellar hemangiomas.

2- Chronic hypoxia (PaO_2 < 60 mmHg): It produces **relative polycythemia.**

For example: • Chronic obstructive pulmonary disease (COPD).
• High altitudes (>7000 feet), humans are at risk of both acute and chronic mountain sickness disease, which is manifested by severe headache, nausea, vomiting, and disorientation due to cerebral edema.
• Cigarette smoking (increased carboxy-Hb> 5-7%).
• Congenital heart diseases.
• Pickwickian syndrome.

3- Abnormal Hb: It produces **relative polycythemia.**

For example: • Met-hemoglobinemia.
• Abnormal Hb with increased O_2 affinity to heme moiety, due to abnormal Hb mutations such as Hb Chesapeake, J-Capetown, Kemsey, and Creteil. They cause shift of O_2-Hb dissociation curve to the left. Accordingly, they deliver less O_2 to tissues and cause tissue hypoxia at normal capillary PaO_2.

Clinical Picture:

• **Ruddy cyanosis, injected conjunctiva, pruritis, and splenomegaly.**
• Increased Hb level, which increases **blood viscosity** resulting in **compromising O_2 delivery and increasing risk of arterial and venous thrombosis** according to the level of Hct.
  ▫ At Hct between 33-36% (Hb of 11-12 g/dL), tissue O_2 delivery (and tissue perfusion) is maximal.
  ▫ At Hct between 36-50%, the effect is relatively minor.
  ▫ **At Hct between 50-60%,** the O_2 delivery (and tissue perfusion) to vital organs is compromised with greatly increased risk of arterial and venous thrombosis.
  ▫ At Hct > 60%, a life threatening condition is produced due to severely decreased tissue perfusion.
• A possibility of increased risk of **bleeding diathesis (tendency)**. The cause of bleeding diathesis is due to an acquired von Willebrand disease because hyper-viscosity favors conformational changes in von Willebrand factor that render it vulnerable to enzymatic cleavage.
• 15% of patients develop **acute leukemia**.

Anesthetic Problems:

1- Elective surgery should be **postponed until the Hct becomes < 50%.** Reduction of blood viscosity should be performed by: • **Fluid administration** with care to avoid severe hemodilution as it may lead to mild anemia.
• **Repeated regular phlebotomies** may be performed.

2- **Myelo-suppressive drugs**, used for polycythemia vera, produce side effects, which should be detected and managed preoperatively.

Disorders of Coagulation (Hemostasis) and Clotting Factors

Physiological Considerations

• Hemostasis is the balance between the coagulation systems, which forms the blood clot, and the anticoagulation system which limits the blood clot formation. Normally the blood components are in balance maintaining hemostasis.
• Normally, intact endothelium of blood vessels prevents activation of hemostatic mechanisms. It is protected from spontaneous thrombus formation by:

1- The constitutive expression of native anticoagulants such as:
  ▫ endogenous heparin sulfate, which increases the activity of antithrombin and thrombomodulin,
  ▫ tissue factor pathway inhibitor (TFPI), and
  ▫ tissue plasminogen activator (tPA).

They are discussed later.

2- Release of nitric oxide, prostacyclin, and tissue plasminogen activator intravascularly from endothelial cells to enhance blood flow.

Coagulation

Stimulus:

Coagulation is initiated almost instantly after physical (surgery or trauma), chemical, or cellular injury to the vascular endothelial lining of blood vessels, which activates the local endothelium promoting inhibition of the anticoagulant molecules and also stimulation of the procoagulant molecules. This leads to vascular spasm, primary hemostasis, and secondary hemostasis.

Vascular Spasm:

- After injury of blood vessels, the wall of the cut blood vessel immediately contracts, which serves to decrease blood loss from the damaged vessels. This contraction results from:
  - neural reflexes initiated by pain impulses from the traumatized vessel and
  - release of vasoconstricting substances such as serotonin and thromboxane A_2 from platelets.
- Vascular spasm lasts 20-30 minutes, providing time for additional mechanisms of hemostasis to become active.
- Vascular spasm is most intense in severely traumatized or crushed blood vessels and is weakest in sharply cut or transected blood vessels as occurs during surgery.
- After vascular spasm, two coagulation processes occur; primary hemostasis and secondary hemostasis.

Primary Hemostasis:

- It involves immediate formation of **a primary hemostatic platelet plug** at the site of blood vessel injury due to the function of platelets. Platelets are changed from dormant to activated platelets (figure 30-3).
- Platelets perform three main actions for formation of the primary hemostatic plug:
  - **Platelet adhesion:** is the affinity of platelets to non-platelet surface.
  - **Platelet release reactions:** gives platelets the ability to attract more platelets to the site of injury.
  - **Platelet aggregation:** is the affinity of platelets to one another.
  - **Platelet procoagulant activity:** During platelet plug formation, a membrane phospholipid called **platelet factor 3 (PF3)**, is exposed. PF3 provides a template for orientation and interaction of proteins of the coagulation cascade. The role of platelets is now clearer in coagulation pathway as many of coagulation factors activation occurs on its surface (see later).
- Fibrin formation reinforces the stability of the platelet plug (i.e., aggregated platelets), which undergoes clot retraction and stabilization.

The details of these functions of platelets are discussed in chapter "Pharmacological Adjunct to Anesthesia & Intensive Care".

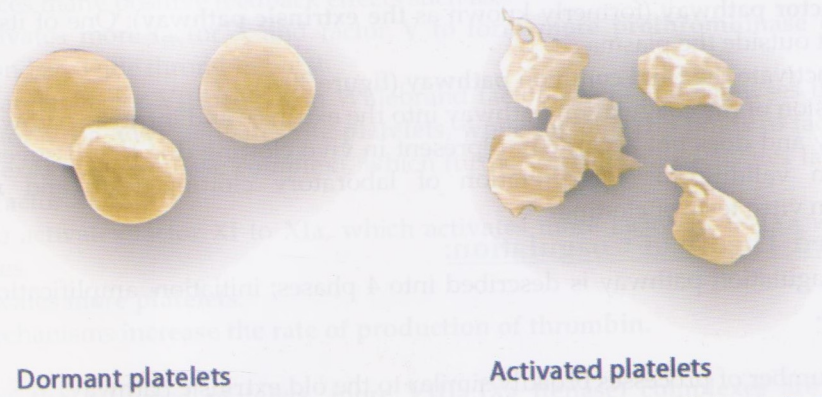


Figure 30-3: Dormant and activated platelets. The activated platelets show cell feet called pseudopodia

Secondary Hemostasis:

- It involves the formation of **a firm hemostatic clot** by reinforcement and strengthening of platelet plug by fibrin strands due to s series of processes that involves activation of many of **coagulation factors**.
- The description of these processes has been changed from old classic coagulation pathway (in vitro) to a new cell-based theory (in vivo).

Coagulation (Clotting) Factors include:

	Name	Half life (hours)
Factor I	Fibrinogen	100
Factor II	Prothrombin	80
Factor III	Tissue thromboplastin	-
Factor IV	Calcium ions	-
Factor V	Labile factor (proaccelerin)	18
Factor VII	Stable factor (proconvertin)	6
Factor VIII	Anti-hemophilic factor (AHF)	10-12
Factor IX	Christmas factor	24
Factor X	Stuart-Prower factor	50
Factor XI	Plasma thromboplastin antecedent (PTA)	25
Factor XII	Contact factor, Hegman factor	60
Factor XIII	Fibrin stabilizing factor	90
Prekallikrein	Fletcher factor	

(There is no factor VI)

• All coagulation factors are synthesized in the liver except factor VIII, which is produced by platelets and megakaryocytes (platelet precursors).

• **Factor VIII** is formed of 2 parts (2 molecules) each under separate genetic control.

	Factor VIII: C	Factor VIII R: Ag
Size	It is the smallest part.	It is the largest part.
Function	It has the coagulant activity.	• It acts as a carrier for factor VIII: C. • It is important for platelet adhesion. • It contains both factor VIII antigen and the Von Willebrand factor (vWF).
Its Defect causes	Hemophilia A	Platelet dysfunction and von Willebrand disease
Both parts are present together in the plasma as a complex.		

• Factors V and VIII are called labile factors because their coagulant activity does not last long in stored banked blood, so packed RBCs are deficient in these factors. In fresh frozen plasma, factor VIII concentration is decreased in comparison to fresh pooled plasma.

The Classic Coagulation Pathway:

Classically, the coagulation cascade has two pathways:

1- **The contact activation pathway** (formerly known as **the intrinsic pathway**): All its components circulate in the plasma.

2- **The tissue factor pathway** (formerly known as **the extrinsic pathway**): One of its components (tissue factor) is present outside the plasma.

Both pathways activate **the final common pathway** (figure 30-4).

• The rigid division of the coagulation pathway into the extrinsic and intrinsic pathways has actually lost absolute validity and does not accurately represent in vivo clotting due to crossover of many factors. It still has certain validity for interpretation of laboratory clotting tests and remains useful for understanding in vitro tests of clotting.

The Cell-Based Theory of Coagulation:

Recently, the coagulation pathway is described into 4 phases; initiation, amplification, propagation and clot stabilization.

1- Initiation:

• It involves a number of processes broadly similar to the old extrinsic pathway.

• At the site of vascular injury, **subendothelial tissue factor (TF)** is exposed to circulating **factor VIIa** (which is already present in small amounts in the circulation as a free factor) and forms a TF:VIIa complex. This **TF:VIIa complex** activates factor IX and X to active factor IX (IXa) and active factor X (Xa). Factor **IXa binds to platelets**, while **factor Xa** activates factor V to active factor V (**Va**) and forms with it **Xa:Va complex called prothrombinase complex,** which converts localized, **small amounts of prothrombin to thrombin**. This **small amount of thrombin** serves as a primary mechanism for the clotting process that initiates coagulation and **activates platelets** (to perform their release reactions).

• There is then further activation and assembly of coagulation factors on the platelet surface, but until this stage the quantities of thrombin and coagulation factors activated are very small.

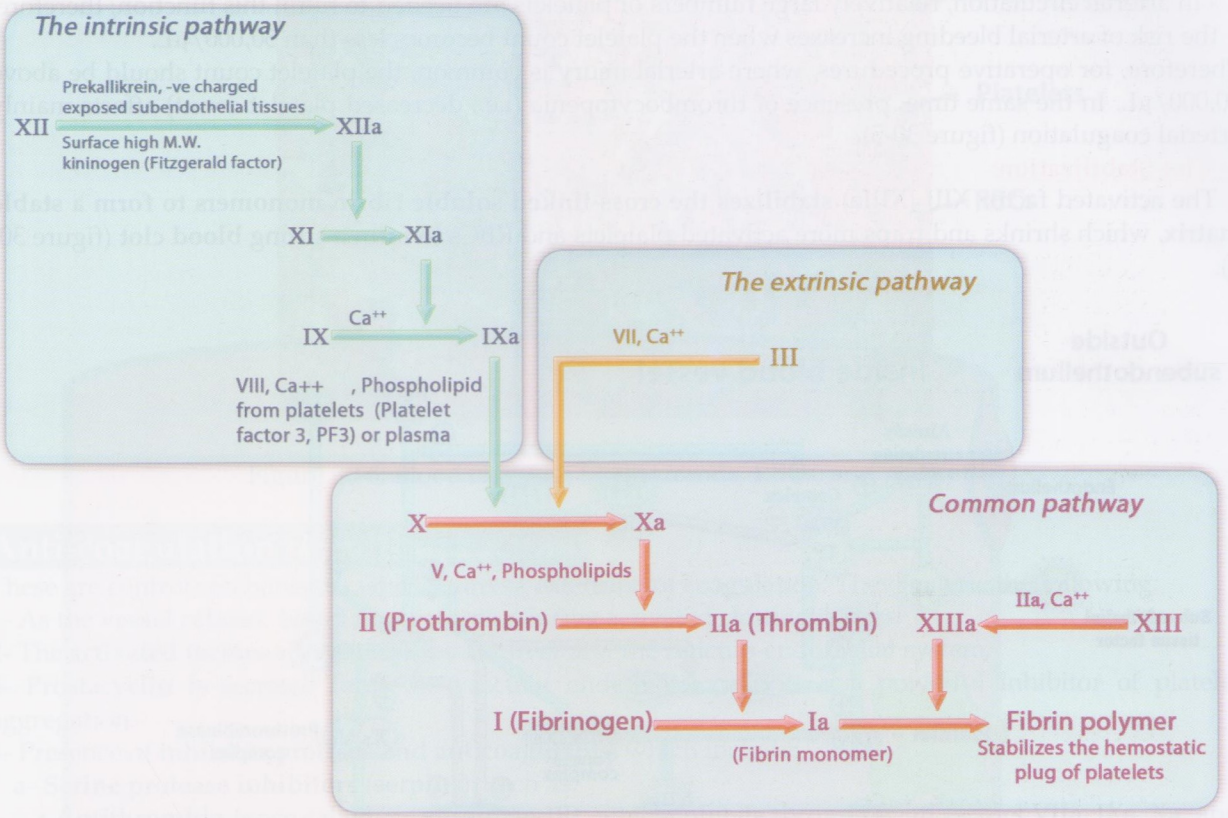


Figure 30-4: The classic traditional coagulation pathway

2- Amplification:

• This phase involves numerous **positive feedback mechanisms**, which produce more activation and assembly of the coagulation factors. These positive feedback mechanisms include:

- **Factor VIIa** has a positive feedback effect on itself resulting in **further activation of TF:VIIa complex.**
- **Thrombin** produces many positive feedback effects such as:
  1. Thrombin activates more factor X and factor V to form **more prothrombinase complexes** that generate the secondary wide thrombin burst.
  2. Thrombin separates factor VIII from von Willebrand factor (vWF) and catalyses the activation of factor VIII to factor VIIIa. **vWF activates the platelets**, while **factor VIIIa** binds to factor IXa to form **VIIIa:IXa complexes** (called **tenase complex**), which further recruits and activates factor X from the plasma to **more factor Xa.**
  3. Thrombin also activates factor XI to **XIa**, which activates more factor IX to **IXa** with the help of TF:VIIa complexes.
  4. Thrombin activates **more platelets**.

• These feedback mechanisms **increase the rate of production of thrombin.**

3- Propagation:

• **On the surface of the activated platelets, more VIIIa:IXa (tenase) complexes** are formed, which produce more and **more Xa:Va (prothrombinase) complexes.** This process requires platelet factor 3 and calcium.

• Therefore, additional thrombin is produced (sometimes called **thrombin burst**), which is **now sufficient to generate fibrin from fibrinogen** and **activate factor XIII to factor XIIIa.**

N.B.:

• Thrombin plays a major role during amplification and propagation of clot formation.

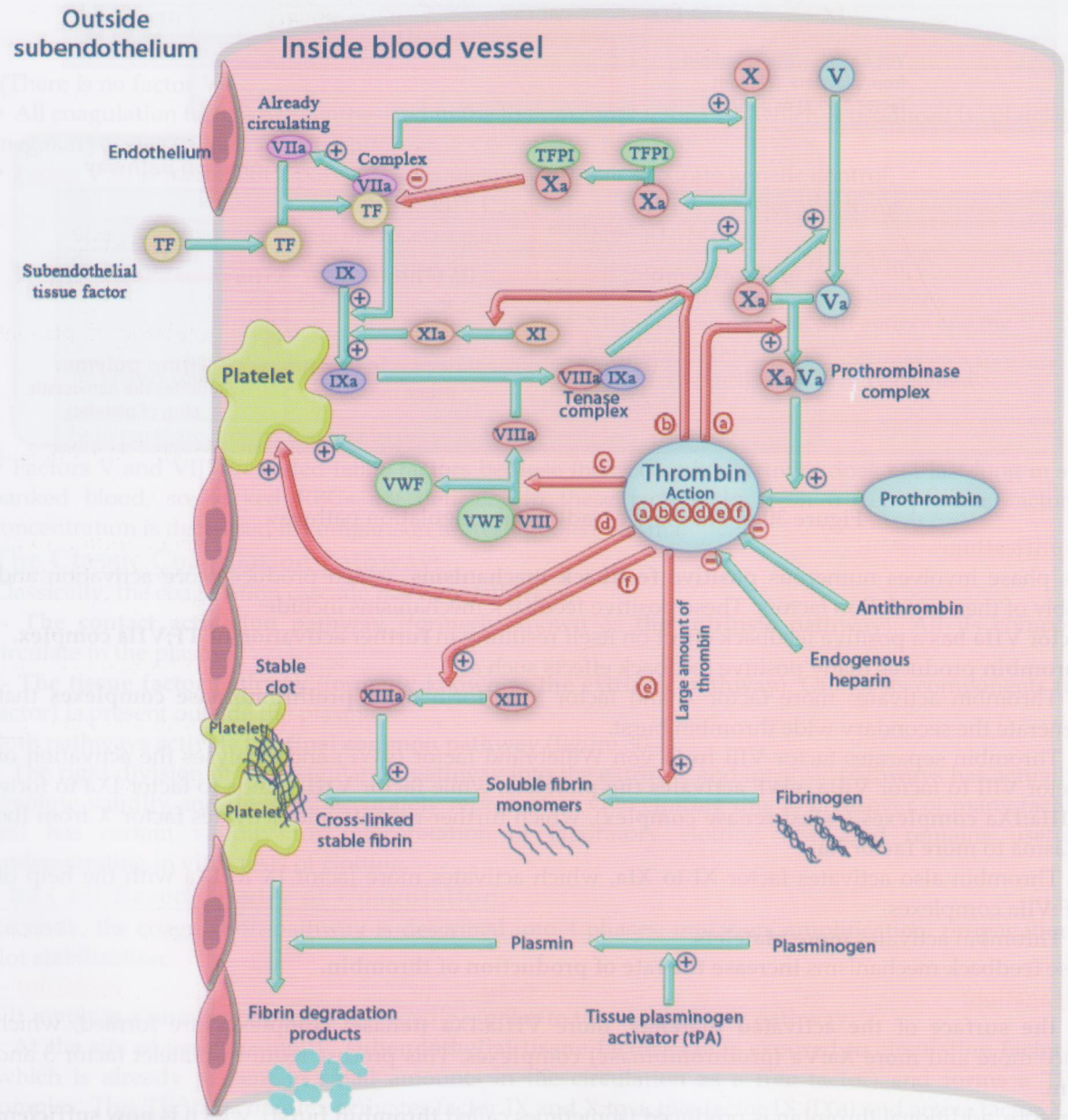
• The platelets play also a major role in formation of the clot as the coagulation cascade assembly on the platelet surface. There is a difference between the arterial and venous circulation:

- In venous circulation, relatively small numbers of platelets are needed to fulfill this function; therefore, the risk of venous bleeding only increases when the platelet count becomes very low i.e., less than 10,000/μL.
- In arterial circulation, relatively large numbers of platelets are needed to fulfill this function; therefore, the risk of arterial bleeding increases when the platelet count becomes less than 50,000/μL.

Therefore, for operative procedures, where arterial injury is common, the platelet count should be above 50,000/μL. In the same time, presence of thrombocytopenia (i.e., decreased platelet count) affects mainly arterial coagulation (figure 30-5).

4- Clot Stabilization:

• The activated factor XIII (XIIIa) **stabilizes the cross-linked soluble fibrin monomers to form a stable matrix**, which shrinks and **traps** more activated platelets and RBCs to form **a strong blood clot** (figure 30-6).



TF Tissue factor
VWF Von Willbrand factor
TFPI Tissue factor pathway inhibitor

Figure 30-5: The new coagulation cascade

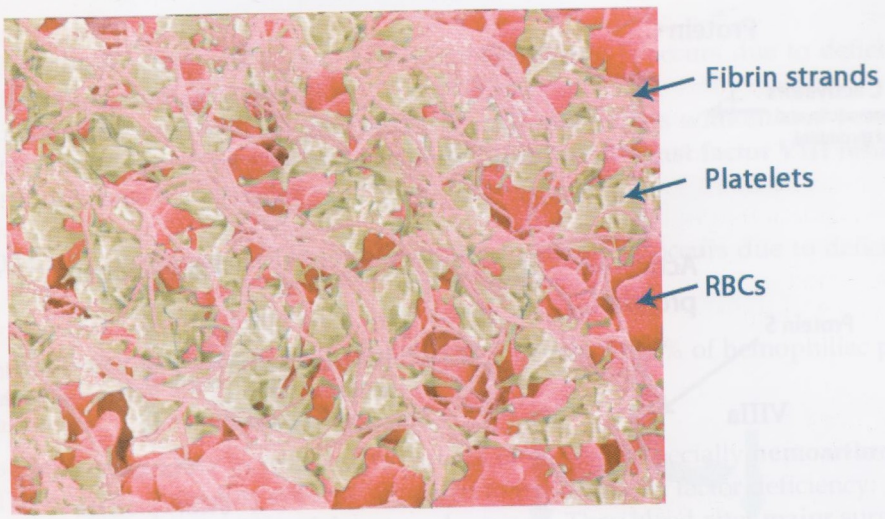


Figure 30-6: Blood clot with fibrin strands, RBCs, and platelets

Anti-coagulation (Limiting Factors)

These are control mechanisms, which prevent extension of coagulation. They include the following:

1- As the **vessel relaxes**, blood flow returns diluting activated clotting factors.

2- The **activated factors** are removed by the liver and the reticulo-endothelial system.

3- **Prostacyclin** is secreted form the vascular endothelial cells. It is a powerful inhibitor of platelet aggregation.

4- Presence of **inhibitor proteins and anticoagulants**, which include:

a- **Serine protease inhibitors (serpins):** such as:

- **Antithrombin** (once called antithrombin III), which inhibits thrombin and factors VIIa, IXa, Xa, and XIa. It is synthesized by the liver.
- **Heparin cofactor II**.

Endogenous heparin sulfate found on the endothelial cell surface speeds the action of antithrombin 1000-fold in presence of heparin cofactor II, and normally protects normal endothelium from spontaneous thrombus formation.

b- **α_2-Macroglobulins**: They trap, inactivate, and rapidly clear circulating activated coagulation factors.

c- **Tissue factor pathway inhibitors (TFPI):** It is a protein that binds to factor Xa forming a complex, which inhibits TF:VIIa complex.

d- **Thrombomodulin** is an endothelial membrane protein receptor that **binds thrombin** and alters the thrombin molecule. **Altered thrombin** activates **protein C** (vitamin K dependent protein), which inactivates factor Va and factor VIIIa. It also inactivates an inhibitor of tissue plasminogen activator (tPA), increasing the formation of plasmin. **Protein S** acts as a cofactor and accelerates the action of protein C.

5- **Fibrinolytic System**:

Fibrinolytic system is responsible for **fibrin clot dissolution.** It comprises the following:

- Plasminogen is activated to plasmin (an active protease enzyme), which splits the fibrin thrombus to fibrin degradation products and D-dimer.
- The tissue plasminogen activator (tPA), derived from injured endothelium, stimulates conversion of plasminogen to plasmin, while plasminogen activator inhibitor type 1 prevents activation of plasminogen.
- α_2 antiplasmin inhibits the action of plasmin (figure 30-7).
- If the fibrin degradation products are produced at a rate that exceeds their normal clearance from the blood by the liver, kidney, and reticulo-endothelial system, they will accumulate in the blood reaching high concentrations. They then act as anticoagulants through impairing platelet function, inhibiting thrombin, and preventing the cross-linkage of fibrin strands and lead to bleeding as seen in disseminated intravascular coagulopathy (DIC).

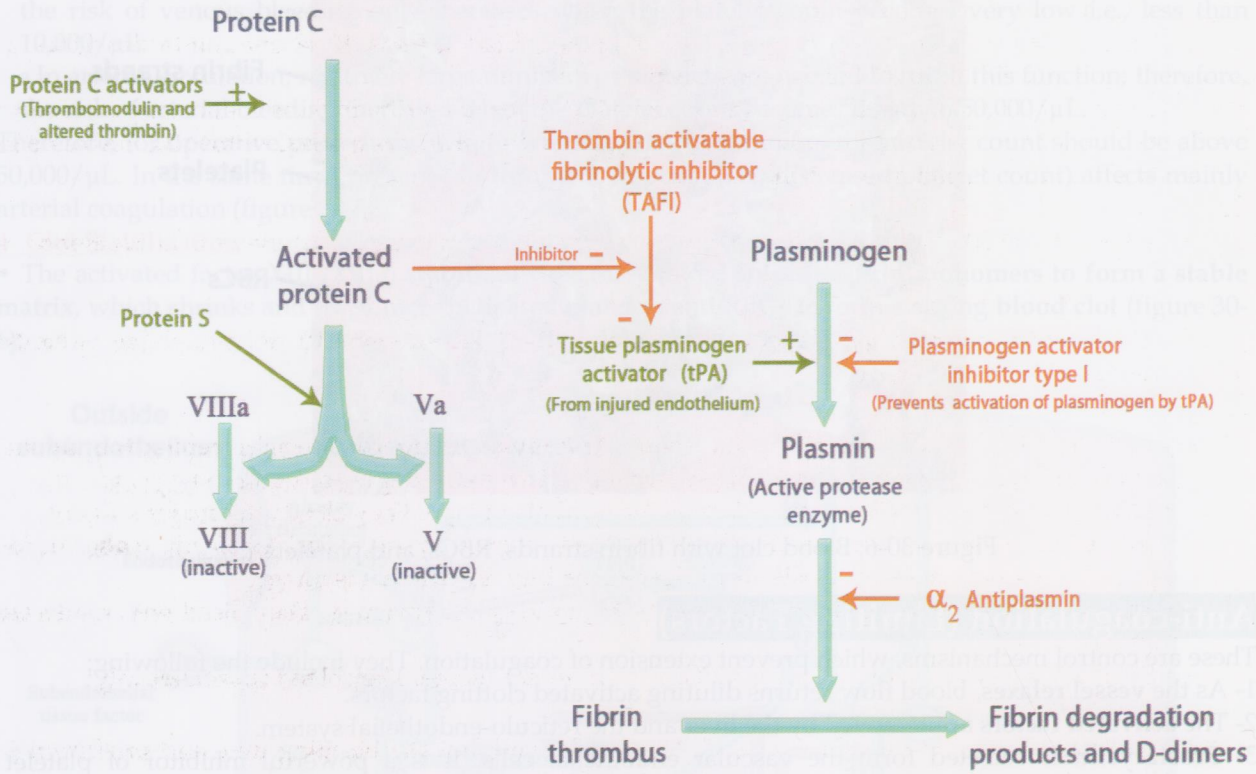


Figure 30-7: The fibrinolytic system

Hypocoagulability

It includes:

a- Hereditary (heritable or congenital) disorders:

- Deficiency of factors VIII and IX (Hemophilia).
- Deficiency of von Willebrand factor.
- Fibrinogen abnormalities:
  - Deficiency of fibrinogen (afibrinogenemia),
  - Hypofibrinogenemia, and
  - Dysfibrinogenemia.
- Deficiency of factors II (prothrombin), V, VII, X, XI, and XIII.
- Hereditary hemorrhagic telangiectasia.

b- Acquired disorders:

- Vitamin K deficiency
- Liver disease.
- Inhibitors of coagulation.
- Drug induced hemorrhage (therapeutic anticoagulant drugs).
- Dilution of procoagulants and massive blood transfusion.
- Disseminated intravascular coagulopathy (DIC).

a- Hereditary Hypocoagulability Disorders

Hemophilia

It is a **sex-linked recessive** disorder, affecting **males mainly.**

Hemophilia does occur **in females** owing either to:

- early X chromosome inactivation of the normal X in a heterozygous female or
- inheritance of two abnormal X chromosomes (one from an affected father and one from a carrier mother).

10% of female carriers have factor VIII activity < 30 % and are at risk of bleeding with surgery.

Types:

Hemophilia A (Classical Hemophilia):

Its incidence is 1:10 000 males. It represents 85% of hemophiliac patients. It occurs due to deficiency of factor VIII: C (a qualitative and quantitative defect).

N.B.: **Hemophilia-like syndrome** may occur in genetically normal individuals without any personal or family history of abnormal bleeding due to **acquired antibody inhibitors against factor VIII** resulting in sudden onset of severe spontaneous hemorrhage.

Hemophilia B (Christmas Hemophilia):

Its incidence is 1:100 000 males. It represents 14% of hemophiliac patients. It occurs due to deficiency of factor IX.

N.B.: **Hemophilia C (Rosenthal's Disease):**

Some authors consider **deficiency of factor XI** as hemophilia C. It represents 1% of hemophiliac patients. It is an autosomal recessive disease.

Clinical Picture:

All hemophilic patients **bleed** excessively in response **to trauma or surgery** especially **hemoarthrosis and deep tissue bleeding**. The degree of bleeding severity is related to the degree of factor deficiency:

- **Mild cases** have factor VIII level **> 30%** of the normal average. They bleed after **major** surgery.
- **Moderate cases** have factor VIII level **6-30%** of the normal average. Besides bleeding after major surgery, they show **hemoarthrosis, deep tissue bleeding, muscle hemorrhage**.
- **Intermediate cases** have factor VIII level **1-5%** of the normal average. They bleed with **moderate** trauma.
- **Severe cases** have factor VIII level **< 1%** of the normal average. They bleed **spontaneously**.

Investigations:

- **Activated partial thromboplastin time (aPTT) is prolonged,** but the bleeding time and prothrombin time (PT) are normal.
- The level of factor VIII (in hemophilia A) or factor IX (in hemophilia B), is decreased.

Treatment:

Factor VIII (in hemophilia A) or factor IX (in hemophilia B) replacement is the main line of treatment. Desmopressin is also used.

1) By Factor VIII (or IX) Replacement Therapy:

Indications:

1- Uncontrolled bleeding.

2- Preoperative preparation for elective surgery.

Aim:

a- In Hemophilia A: Although > 30% factor VIII level is adequate, but reaching **100%** of factor VIII is the ideal **1-2 hours before surgery** (due to presence of antibodies), then factor VIII level is to be maintained as follows: • > 80%, during the 1st 4 postoperative days,

- > 40%, during the next 4 days,
- > 10%, during the next 3 weeks (in severe cases).

Other centers maintain factor VIII level **> 50% during the 1st 10-14 postoperative days.**

b- In Hemophilia B: reaching **> 30%** of factor IX level perioperatively is enough to maintain hemostasis.

Calculation of the Dose:

One unit of factor VIII activity/kg body weight increases plasma factor VIII level about 2%.

For example: a 70 kg hemophiliac man with 10% factor VIII, needs to reach 100% factor VIII activity.

Factor VIII is needed to be elevated as follows 100 – 10 = 90

Therefore, $\frac{90\%}{2\%}$ x 70 Kg = 3150 units of factor VIII are needed to be infused.

N.B.:

- **One unit of factor VIII activity** is defined as the amount of factor VIII present in one mL of fresh normal pooled plasma.
- **One% of factor VIII** = 0.01 U/mL.

Interval of Administration:

- For hemophilia A, **factor VIII** is administered **every 12 hours** (as the $t_{1/2}$ of factor VIII is 10-12 hours). **In children**, the half-life of factor VIII may be as short as **6 hours**, needing more frequent infusions.
- For Hemophilia B, **factor IX** is administered **every 24 hours** (as the $t_{1/2}$ of factor IX is 18-24 hours).

Route of Administration:

a- **I.v. bolus** administration (not preferred).

b- **I.v. infusion** is **preferred** and **more effective** because:

- This **eliminates the high peak concentration** observed after bolus injection.
- It **avoids inhibition by antibody inhibitors** (see later) because most of the inhibition occurs after 1-2 hours of factor VIII administration. On continuous infusion, some of factor VIII will circulate and is still active.

Forms of Factor VIII and IX:

1) Fresh Frozen Plasma (FFP):

- It contains **0.7-0.9 unit** of factor VIII activity/mL.
- There is risk of transmission of: ▫ hepatitis B virus infection (1: 200 000),
  ▫ hepatitis C virus infection (1: 3300), and
  ▫ human immunodeficiency virus infection (AIDS) (1: 450 000-660 000).

2) Cryoprecipitate:

- It is the fraction of plasma that precipitates when FFP is thawed.
- It contains **5-13 units** of factor VIII activity/mL.
- Advantages: ▫ Readily available.
  ▫ Long shelf life.
  ▫ Relatively low risk of hepatitis and AIDS (but still present).
  ▫ It contains also fibrinogen, fibronectin, and vWF.
- Disadvantages: ▫ Allergic reactions.
  ▫ Rh sensitization; because it contains RBCs fragments, which can sensitize Rh negative individuals to Rh antigens if the donor is Rh positive.

3) Human heated-Treated Lyophilized Purified Factor VIII (or Factor IX) Concentrate (*Koate DVI*)**:**

- It contains **50-100 units** of factor VIII activity/mL.
- Advantages: ▫ Easily stored and reconstituted.
  ▫ Long shelf life.
  ▫ Known potency.
- Disadvantages: ▫ Still the risk of hepatitis and AIDS is present but reduced.

4) Recombinant or Monoclonal Purified Factor VIII (or Factor IX):

- Advantages: ▫ There is no risk of hepatitis or AIDS (biologically safe).
  ▫ Stable.
- Disadvantages: ▫ High cost.

N.B.: **10-30% of hemophilic A** patients and **5% of hemophilic B** patients have **antibody inhibitors** against factors VIII, and thus the anticipated response from transfusion therapy is not achieved. Therefore, the following measures should be done:

1. Preoperative measurement of **antibody (IgG) titre** is important.
2. Preoperative measurement of Bethesda unit of inhibition is important.

Bethesda unit of inhibition is the amount of inhibitory antibody activity that decreases factor VIII level in one mL of normal plasma from one to 0.5 unit.

3. **Mixing study:** is required to detect the presence of an inhibitor.

Technique: Mixing patient plasma and normal plasma in a 1: 1 ratio is performed and then the correction (shortening) of the prolonged PTT is determined.

Results: ▫ In classic hemophilia A patients with a deficiency in factor VIII activity, but no circulating VIII inhibitors, the mixing study shows shortening of the PTT to within 4 seconds or less of the normal PTT control.
▫ In Patients with factor VIII inhibitors, the PTT will not be shortened to that extent, if at all.

Therefore:

a- Patients with **low antibody titre and low Bethesda unit** (< 10 U/mL), will benefit form factor VIII transfusion.

b- Patients with **high antibody titre and high Bethesda unit** (> 10 U/mL), will get no or minimal benefit from factor VIII transfusion. These patients are managed as follows:

1- Recombinant factor VIIa (*Novoseven*): It is the **treatment of choice**.

Action: Hemophiliacs can generate Xa via factor VIIa binding to tissue factor in the initiation phase and in the propagation phase. They are unable to generate Xa and the subsequent thrombin burst on the platelet surface in the absence of factor VIII or IX. Recombinant factor VIIa in high concentrations

appears to essentially replace the VIIIa/IXa tenase complex requirement by binding to the platelet surface and increasing both Xa generation and the thrombin burst, unaffected by factor VIII or IX inhibitors.

Dose: For active bleeding of patients with inhibitors, a dose of 90-120 μg/kg i.v. is recommended every 2-3 hours until hemostasis is achieved or according to the coagulation test.

2- Massive factor VIII concentrate may be given, but it is a temporary measure.

3- Plasmapheresis may be tried first then **factor VIII** is given. It is also a temporary measure.

4- Activated prothrombin complex concentrates *(Octaplex or Beriplex).*

5- Porcine factor VIII (of animal source) is effective if the Bethesda unit is < 50 U/mL. Its dose is 100-150 U/kg.

N.B.: Immuno-suppressive therapy is of no value.

2) Desmopressin (1-desamino-8-D-arginine vasopressin "DDAVP"):

Action: It is a synthetic analogue of antidiuretic hormone (ADH), which causes release of factor VIII: C from endothelial cell storage sites. It increases concentration of factor VIII 2-6 times and vWF 2-4 times within 30 minutes of injection.

Indication: It is effective and may completely eliminate the need for blood products in mild bleeding episodes or during minor dental or surgical procedures and may decrease the amount of blood products required for major bleeds or surgical procedures.

Dose:

- 0.3 μg/kg i.v. or intranasal 30 minutes before the surgery. It should be diluted in 30-50 mL of saline and infused over 10-20 minutes to minimize side effects. It is usually used once.
- 1.5 mg/mL nasal spray every 24-48 hours.

Disadvantages:

- On rapid injection; tachycardia, hypotension, headache, nausea, and facial flushing.
- It cannot be repeated because such stores become depleted.
- It also releases tissue plasminogen activator (tPA); therefore, epsilon amino-caproic acid or tranexamic acid is recommended with it.

Anesthetic Problems:

1- Elective surgeries (even minor) should be carried out only in **designated hemophilia centers,** which have the staff, technical facilities and experience necessary to supervise and manage these patients.

Emergency surgeries should be done under the advice and supervision of a hematologist at the nearest designated center.

2- Preoperative management should be performed as above.

3- Premedications: Avoid all i.m. injections. Only use oral or i.v. routes (although factor VIII activity > 30-50% is considered safe for i.m. injections).

3- 25% of hemophilic patients have antibodies to **human immunodeficiency virus (HIV) and hepatitis virus**; so, take all precautions (e.g., avoid drugs that affect liver disease in anesthesia).

4- Avoid any trauma during anesthesia such as:

- All forms of **regional anesthesia are contraindicated** (there are some reports of succeeded axillary block in these patients).
- During airway management,
  - Careful **placing of the mask is needed** to avoid pressure trauma to the lips, tongue, and face.
  - **Laryngoscopy** is done **after complete muscle relaxation** only by **skilled clinician** using a **curved blade (less traumatic).**
  - **An endotracheal tube** should be **small and well lubricated**.
  - **Nasal intubation** should be **avoided.**
  - **Gentle oral suction** should be done under direct vision before extubation should be done.
- Postoperative pain control: **Avoid non-steroidal anti-inflammatory drugs (NSAIDs)**. Opioids or paracetamol can be used safely.
- **Postoperative factor VIII concentrate maintenance** should be done as above. It is given while the patient is in the hospital or at home.

Von Willebrand's Disease

Types:

	Incidence	Mode of Inheritance	Type of the Defect	Severity of Clinical Picture
Type 1	80% of cases (the most common)	Autosomal dominant	**A quantitative defect** in the vWF. There is usually a mild decrease in the level of vWF activity to 15-30% of normal	Mild
Type 2	15-20%	Autosomal dominant	**A qualitative defect** in factor vWF.	Moderate
Type 3	Very rare	Autosomal recessive	**A quantitative defect** in factor VIII C and vWF complex. There a decrease in vWF and factor VIII to 3-10% of normal.	Severe

Incidence: 2-3% heterozygous trait (**the most common inherited** bleeding disorder).
1: 10 000 homozygous trait (as hemophilia A).

Clinical Picture: As hemophilia A.
Bruising and mild bleeding on trauma (e.g., epistaxis) or after surgery, but hemoarthrosis and deep tissue bleeding are uncommon.
Pregnant women with vWF disease show vaginal bleeding without excessive bleeding because pregnancy increases vWF in the plasma.

Investigations:
1- Prolonged bleeding time, but normal platelet count.
2- Decreased vWF concentration (Normal vWF concentration in plasma = 5-10 mg/L).
3- Decreased Factor VIII activity as vWF acts as a carrier for it; therefore, PTT is prolonged.
4- The pathognomic diagnostic test for von Willebrand's disease is the immediate rise in factor VIII levels following infusion of plasma. These levels continue to rise up to 48 hours in patients with von Willebrand's disease, in contrast to the fall seen in patients with hemophilia.

Treatment:
1- vWF replacement: by fresh frozen plasma, cryoprecipitate, or factor VIII concentrate.
2- Desmopressin (DDAVP): It evokes the release of vWF from storing sites (see before). It produces good response to type 1, uncertain response to type 2, and no response to type 3.

Other Hereditary (Congenital) Coagulation Disorders

Types:

Hereditary Disease	Mode of inheritance
Afibrinogenemia (congenital absence of fibrinogen) and hypofibrinogenemia	Autosomal recessive
Dysfibrinogenemia (production of abnormal fibrinogen)	**Autosomal dominant**
Factor II deficiency	Autosomal recessive
Factor V deficiency	Autosomal recessive
Factor VII deficiency	Autosomal recessive
Factor X deficiency	Autosomal recessive
Factor XI deficiency (hemophilia C or Rosenthal's disease)	Autosomal recessive
Factor XII deficiency	Autosomal recessive
Factor XIII deficiency	Autosomal recessive

These factor deficiencies are either hereditary diseases (gene related as above) or congenital diseases (due to mutational changes).
N.B.: **Difference between hereditary and congenital diseases:** Both occur since birth, but:

- **A hereditary (inherited, heritable, genetic, or familial) disease or disorder** is the **genetically predetermined** disorder. It is dependent on the genetic material or chromosomes that a person inherits from one or both biological parents.
- **A congenital disorder** is the disorder that is **present since birth due to intrauterine pathology** during development. It may be **inherited** abnormalities, or it may occur due to **a spontaneous mutation** in the chromosomes. It also may be due to **environmental influences** (i.e., **non-chromosomal disorder**) during pregnancy such as exposure to harmful chemicals or infectious agents e.g., congenital syphilis.

Clinical Picture

Generally, • **Bleeding usually occurs after trauma** e.g., cutting the umbilical cord or surgery. It is usually superficial and can be controlled after local compression.
• **Petechiae**: small (pinpoint) hemorrhages from capillaries in the dermis.
• **Thrombo-embolic complications** may occur in **factors I (fibrinogen) deficiency, factor VII deficiency, and factor XII deficiency.**

Investigations:

1- The Coagulation Screen Tests:

The old classical pathway (see above) is still useful for interpretation of laboratory clotting tests as follows:

- The intrinsic pathway involves activation of factors VIII, IX, XI, and XII. It is assessed by activated partial thromboplastin time (aPTT).
- The extrinsic pathway involves activation of factors III and VII. It is assessed by prothrombin time.
- The common pathway involves activation of factors I (fibrinogen), II (prothrombin), V, and X. it is assessed by thrombin time (TT).

Therefore,

- Deficiency of factors VIII (hemophilia A), IX (hemophilia B), XI (hemophilia C), and XII prolongs aPTT only.
- Deficiency of factor VII prolongs PT only.
- Deficiency of factors I, II, V, and X prolongs PT, aPTT, and TT.

Deficiency of factors I, II, and V also prolongs the bleeding time due to the interaction of these factors and platelet function in supporting clot formation.

- Deficiency of factor XIII. Although bleeding diathesis occurs, its deficiency does not prolong any coagulation screening test because only a small amount (1-3%) is needed to maintain normal hemostasis.

2- Functional Assays for the Suspected Deficient Factors can be done.

Treatment:

1- Factor Replacement:

Generally, in hereditary coagulation factor deficiencies, the coagulation level required for normal hemostasis is 25-30% of the normal level. This can be achieved by:

1. **Factor concentrate** for the specific deficient factor. It is either • **purified heated- treated factor or** • **recombinant factor**
2. **Cryoprecipitate** (if factor concentrate is unavailable)
Dose: one unit for every 10 kg body weight initially then 25% of the previous dose/day.
3. **Fresh frozen plasma (FFP):**
10-15 mL/kg initially then 5-10 mL/kg/day.
4. **Purified prothrombin complex concentrates (PCC):**
It can be used in many of factor deficiencies such as factors II, V, VII, IX, and X.
Dose: 20-30 units/kg initially, then 15 units/kg for minor surgery, or 40-60 units/kg for major bleeding or surgery.
Side effects: It may increase thromboembolic complications and DIC.
5. **Specific therapies:** (in addition to the above)

- **In factor V deficiency, platelet transfusion** can be used, because factor V is stored in platelet granules.
- **In factor VII deficiency,**
  - **Proplex T** (factor IX complex) can be used due to its high content of factor VII.
  - **Recombinant factor VII** (*Novoseven*) is used.
- **In factor XI deficiency, recombinant factor VII** (*Novoseven*) can be used.

N.B.: **Factor XII deficiency**, is usually associated with no or very mild clinical picture; therefore, it usually requires **no treatment**.

2- Adjuncts to Factor Replacement Therapy:

1. **Desmopressin** (see above).
2. **Antifibrinolytic agents** such as amino-caproic acid and tranexamic acid.
3. **Topical hemostatic agents** such as fibrin glue and fibrillar collagen preparations applied directly to local areas of mucosal bleeding such as epistaxis.

Hereditary Hemorrhagic Telangiectasia (Osler-Weber-Rendu Syndrome)

It is an autosomal inherited disorder causing **abnormal vasculature,** which leads to:

- **An arteriovenous fistula in the lung** resulting in **high cardiac output failure, hypoxemia, and paradoxical air embolism.**
- Aneurysms in all the **cardiovascular system**, resulting in **hemorrhages** e.g. in the oropharynx, trachea, esophagus, on intubation, or epidural hematomas.

b- Acquired Hypocoagulability Disorders

1- Vitamin K Deficiency:

Vitamin K is a cofactor necessary for the synthesis of functional factors II, VII, IX, and X and protein C and its cofactor S.

Causes of vitamin K deficiency include:

1- Decreased dietary intake as vitamin K is present in green vegetables.
2- Broad-spectrum antibiotics as vitamin K is normally synthesized by bacteria in the intestinal lumen.
3- Biliary obstruction or fat malabsorption as vitamin K is fat-soluble, requiring bile salts for absorption in the intestine.
4- Warfarin derivatives as they inhibit metabolism of vitamin K in the liver and induce a vitamin K-depleted state.
5- Acute or chronic liver disease.
6- Prolonged intake of cholestyramine and mineral oil may interfere with vitamin K absorption.

Investigations: Prolonged PT (++) and aPTT (+) with normal TT and fibrinogen.

Treatment: Vitamin K_1 (phytonadione) 1-10 mg orally, subcutaneously, or intravenously (not intramuscularly). Vitamin K_1 is used for both therapeutic and diagnostic strategy (as in case of vitamin K deficiency correction that occurs within 24 hours).

2- Liver Disease:

- With the exception of vWF and factor VIII, all the coagulation factors and other regulatory proteins (e.g., α_2-antiplasmin, protein C and its cofactor S, and antithrombin) are synthesized in hepatocytes.
- The liver is also the site of clearance of activated coagulation factors and degradation products of fibrin and fibrinogen and is responsible for regeneration of vitamin K after it participates in the synthesis of the vitamin K-dependent coagulation factors.

Investigations: prolonged PT, aPTT, and TT and decreased fibrinogen level.

Treatment: Vitamin K, FFP, and clotting factor concentrates.

3- Inhibitors of Coagulation:

- These inhibitors are immunoglobulins (antibodies) with neutralizing activity directed against specific factors such as inhibitors of factor V and factor VIII.
- For example, certain drug reaction, collagen vascular diseases, malignancy, the use of bovine thrombin preparations, lupus anticoagulant.

4- Dilution of Procoagulants and Massive Blood Transfusion:

It is discussed in more details in the chapter of "Fluid & Electrolyte Disturbances".

5- Drug Induced Hemorrhage (Therapeutic Anticoagulant Drugs): such as:

- Heparin therapy; it prolongs PT (+), aPTT (++), and TT.
- Oral anticoagulants; they prolong PT (++) and aPTT (+).

6- Disseminated Intravascular Coagulopathy (DIC): see below.

7- Traumatic Coagulopathy: see below.

Disseminated Intravascular Coagulopathy (DIC) (Consumption Coagulopathy)

Definition:

It is inappropriate triggering of the coagulation cascade in the flowing blood by specific disease processes.

Pathology:

- **The coagulation cascade is activated** by:

1- Release of **endogenous tissue thromboplastin (tissue factor) or thromboplastin-like substances** from hypoxic acidotic tissues.

2- Direct activation of factor XII by **endotoxins or foreign surfaces** causing widespread deposition of fibrin in the microcirculation leading to:

- **Consumption of coagulation factors and platelets** (i.e., thrombocytopenia).
- **Secondary fibrinolysis** stimulation with changing of plasminogen into plasmin, which digests fibrinogen to fibrin-degradation products and d-dimers.

• **Microangiopathic hemolytic anemia** usually occurs.

• In most cases, the associated process **produces a systemic inflammatory response syndrome (SIRS)** that activates the coagulation producing DIC.

• Activation of coagulation cascade may lead to intravascular fibrin deposition. This progresses to thrombosis of small and midsized vessels, compromising blood supply to various organs and ultimately contributing to multiple-organ dysfunction syndrome (MODS).

Causes: Conditions associated with DIC include:

1- Infections such as **Gram-negative** (more) and Gram-positive bacteria, viruses, malaria, rickettsiae, and tuberculosis.

2- Trauma such as massive tissue injury (crush trauma), head traumas, severe burns, and extensive surgery.

3- Embolisms especially fat embolism or pulmonary embolism

4- Obstetrical complications such as eclampsia, placental abruption, retained placenta, intra-uterine fetal death, septic abortion, placenta previa, and **amniotic fluid embolism.**

5- Malignancy such as acute leukemia, adenocarcinoma, cancer pancreas, or cancer prostate.

6- Toxins such as snake venoms and drugs.

7- Immunological disorders such as severe allergic reaction, hemolytic transfusion reaction (incompatible blood transfusion), or transplant rejection.

8- Metabolic disorders such as severe hypotension (shock), hypoxia, hyperthermia (as malignant hyperthermia), hypothermia, and cardiac arrest.

9- Vascular disorders and prosthetic devices e.g., giant hemangiomas (Kasabach-Merritt syndrome) or aortic aneurysm.

10- Extracorporeal circulation (i.e., cardiopulmonary bypass machine).

All the above conditions also may contribute to severe systemic response syndrome and multiple-organ dysfunction syndrome.

Clinical Picture:

• **It varies in severity** from diffuse **bleeding or a thrombo-embolic** phenomenon, to only a laboratory sign with no clinical manifestations.

• **Bleeding** is usually observed from wound sites and i.v. cannulas.

• It should be considered **a sign of another disease rather than a disease;** so, **the clinical picture of the cause** is present.

• DIC may be associated with **multiorgan dysfunction**. The lungs are commonly involved, and the clinical picture is similar to the **acute respiratory distress syndrome**. Advanced cases are accompanied by **acute oliguric renal failure** and **progressive hepatocellular injury**.

• Sometimes, intravascular thrombosis with skin necrosis and gangrene occurs. This is called **purpura fulminans**.

Investigations:

No single laboratory test definitely identifies DIC.

1- Hypo-fibrinogenemia: serum fibrinogen decreases < 150 mg/dL in severe cases.

2- PT, aPTT, and TT are prolonged due to consumption of clotting factors, especially I, II, V, and VII, and the anticoagulant effects of FDPs.

3- Bleeding time is prolonged due to thrombocytopenia (with **decreased platelet count**) and thrombo-asthenia.

4- Increased fibrin degradation products (FDPs) >40 µg/mL.

5- D-dimers assessment: It can confirm the diagnosis. Once elevated, D-dimers remain increased for days, thus making serial test measurements more sensitive and specific than single measurements.

6- Blood film examination shows **RBC distortion and fragmentation** (i.e., schistocytes) if there is associated micro-angiopathy.

Diagnostic Algorithm for Diagnosis of DIC (Diagnostic Scoring System):

It has a sensitivity of 93% and a specificity of 98%. It comprises 5 steps (figure 30-8):

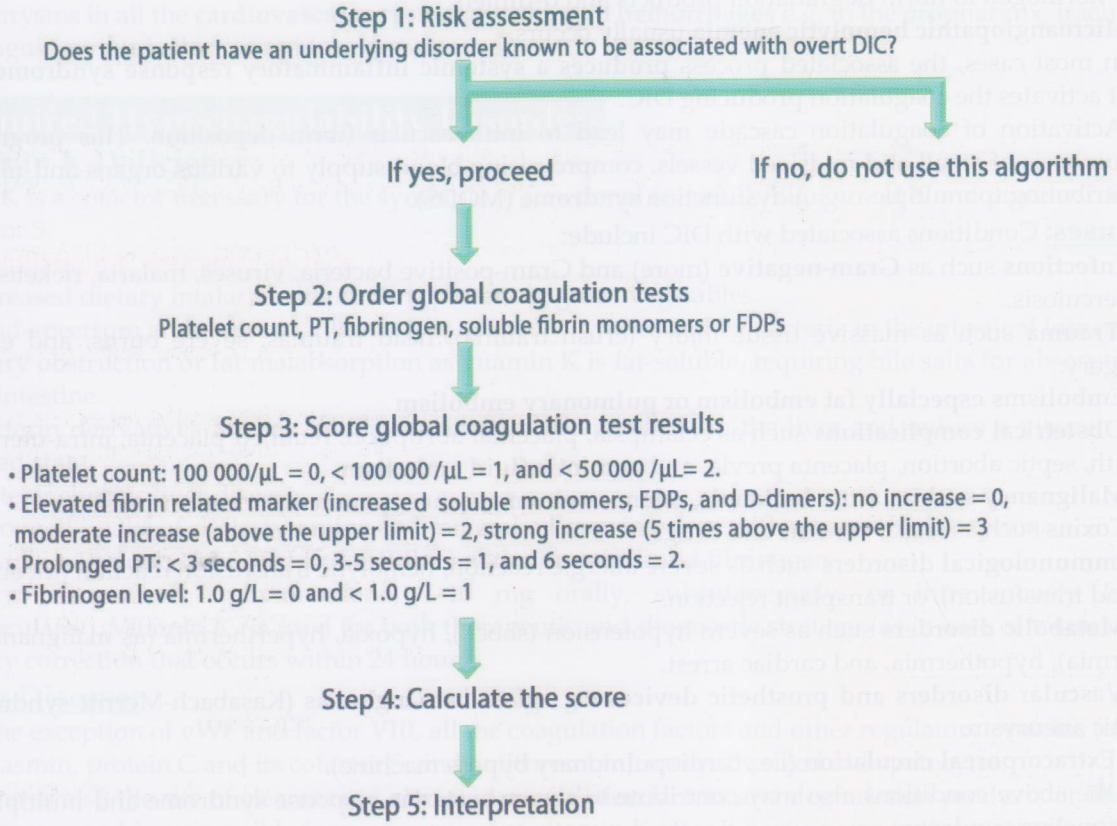


Figure 30-8: The 5-step scoring system

Differential Diagnosis:

1- Other consumption coagulopathies such as:
- localized extra-vascular consumption e.g. placental abruption.
- localized intra-vascular consumption e.g. thrombotic thrombocytopenic purpura.

2- Primary fibrinolysis.

3- Liver disease: coagulation tests, FDPs, and D-dimers are elevated in DIC and liver disease although in liver disease, D-dimer levels may not be as high and platelet counts not as low as that in DIC. Factor VIII activity is helpful in discrimination between these conditions because factor VIII is consumed in DIC and factor VIII levels are normal in liver disease because VIII is not synthesized in liver disease.

Treatment:

1- Treatment of the **cause** e.g., antibiotics for infection, evacuating the uterus, i.v. fluids for shock.

2- Supportive treatment (**replace blood components**) under the advice of a hematologist such as:
- **FFP** is the one preferred because there is a defect in many factors and not one factor only.
- **Cryoprecipitate.**
- **Platelets.**

Coagulation factor concentrates should be avoided because activated factors present in the concentrate may increase intravascular thrombosis.

3- Heparin: is **controversial** as it may be beneficial in patients with thrombo-embolic events or those with clinical sequelae of fibrin deposition such as purpura fulminans.

4- New therapies: They decrease mortality especially DIC due to sepsis.

- **Antithrombin concentrate:** is the physiological inhibitor of coagulation.
- **Activated protein C:** is a naturally occurring anticoagulant system.
- **Recombinant factor VIIa**: used as a salvage therapy in massively bleeding patients with DIC unresponsive to supportive therapy.

Traumatic Coagulopathy

It is responsible for 65% of mortality after trauma.

Causes:

1- Dilutional coagulopathy resulting from the massive hemodilution with plasma expanders and crystaloids. The use of high-molecular weight hetastarch solutions will worsen coagulation by causing dilution of factor VIII causing acquired von Willebrand syndrome.
2- Fibrinolysis that occurs because extensive tissue damage disproportionately increases tissue plasminogen activator.
3- DIC may occur due to consumption coagulopathy.
4- Hypothermia causes slowing of enzymatic reactions in the coagulation cascade and decreases platelet function.
5- Massive blood transfusion syndrome dilutes clotting factors and impairs platelet number ad function.
6- Metabolic abnormalities such as acidosis, hypocalcemia, and increased citrate level also adversely affect the coagulation cascade.

Management:

Recently a new management, which is called "**damage control resuscitation**" is tried with good results. It consists of:
1- The use of blood products as the primary resuscitative fluid in the severely bleeding patient.
FFP is used in 1: 1 or 1: 2 ratio with RBC transfusion with decreasing the use of crystalloids.
2- Aggressive and early re-warming is done.
3- The use of tris-(hydroxymethyl)-aminomethane to treat acidosis is important.
4- Initial surgical control of the bleeding.
5- Early use of recombinant factor VII postoperatively to control coagulopathy. It is not successful if hypothermia, acidosis, and coagulopathy appear.

Perioperative Management of an Anticoagulated Patient

- Patients on oral anticoagulants such as warfarin are at increased risk of perioperative thromboembolism if the drug is stopped, and are at increased risk of bleeding if the drug is continued; therefore, a balance between these two risks should be achieved.
- The recommendation for stopping and restarting warfarin and the use of alternative anticoagulant prophylaxis perioperatively depends on:
  - the severity of the surgical procedure and thus the risk of bleeding and
  - the indication necessitating the warfarin and thus the risk of thrombosis.

Recommendations:

a- For Some Minor Surgeries including skin, dental, and ocular surgery.
They can be performed **without stopping warfarin.**
b- For Elective Major Surgeries:
- **Warfarin** should be **stopped 4 days prior to surgery** to allow the internationalized normal ratio (**INR**) to decrease **below 1.5** (the level thought to be safe for surgery). This is if the INR is normally between 2 and 3. It may take a longer time if the INR is higher.
- **The INR** should be checked **the day prior to surgery** and once the **INR is < 2 alternative pre- and postoperative anticoagulant prophylaxis** should be continued such as i.v. or subcutaneous heparin (or subcutaneous low molecular weight heparin "LMWH"), and **continued postoperatively where warfarin is restarted again until the INR is > 2.** This time for warfarin to be effective again and produce INR > 2 is usually 3-5 days.

Warfarin is replaced by un-fractionated heparin or LMWH because they have shorter actions and they can be replaced by protamine in case of bleeding.

The choice of the alternative anticoagulant prophylaxis is chosen according to its indication and thromboembolic risk as follows:

<table>
<tr><th>Indications and Thromboembolic Risk</th><th rowspan="2"></th><th>Preoperative Management</th><th colspan="2">Postoperative Management</th></tr>
<tr><td><u>Low Risk Patients:</u>
• Atrial fibrillation without embolism
• Valve prosthesis other than mitral or cage prosthesis
• Venous thromboembolic event more than 3 months</td><td>• Low dose subcutaneous heparin 3 days before surgery
• Or subcutaneous LMWH 3 days before surgery either 150-200 U/kg once daily or 100 U/kg twice daily</td><td rowspan="3">Resume warfarin
12 hours after surgery or once surgical hemostasis is felt to be adequate</td><td>• Low dose subcutaneous heparin or LMWH for 3-5 days until INR becomes > 2</td></tr>
<tr><td><u>Intermediate risk:</u>
• Venous thrombosis event < 1-3 month ago
• Atrial fibrillation with history of prior embolism
• Recurrent venous thrombosis</td><td rowspan="2">Stop Warfarin
4 days before surgery. PT should be < 1.5 times control before time of surgery</td><td>As above</td><td>• Low dose i.v. heparin for 3-5 days until INR becomes > 2</td></tr>
<tr><td><u>High risk:</u>
• Venous thrombosis or arterial thrombosis < 1 month ago.
• Mitral or cage prosthesis</td><td>• Full dose i.v. infusion heparin 1000 units/hour to keep aPTT between 1.5-2.5 times normal, 3 days before surgery. I.v. heparin should be stopped 6 hours before surgery.</td><td>• Full dose i.v. heparin for 3-5 days after surgery until INR becomes > 2</td></tr>
</table>

c- For Emergency Major Surgery:

There is too little time to withdraw warfarin and specialist hematological advice should be sought. To reverse oral anticoagulants before surgery in short time, one of the following can be used:

1- **Phytomenadione (vitamin K_1)** (*Konakion, AdcoKion, Amri-K, C & K, Haemokion, Phytovit, or Conadione*):

- Dose: **5 mg i.v.** is usually given, but 0.5-1.0 mg i.v. is sufficient to return INR to its target within 24 hours.
- Duration of reversal: **6-24 hours** (it cannot be hastened by a larger dose). If **excessive vitamin K_1** is given, it may render the patient **refractory** to further warfarinization for days or weeks, so this is not advised.

N.B.: Acetaminaphetone, menadiol, and phytomenadione are all names for vitamin K.
One ampoule vitamin K_1 = 10 mg.

2- If a more rapid reverse is required (for more emergency surgery):

- **Fresh frozen plasma (FFP):** 10-15 mL/kg up to **1 liter (5 units)**, group "O" FFP is used.
- **Vitamin K dependent factor concentrates:** containing factor II, VII, IX, and X at a dose of 50 µg/kg.

It is unwise to fully reverse anticoagulation in patients with prosthetic heart valves. A cardiologist advice is required.

- **Purified prothrombin complex** (*Octaplex or Beriplex*) 50 µg/kg, will correct INR within 20-30 minutes.

d- Recommendations of anticoagulants for regional neuraxial anesthesia

It is discussed in chapter "Regional & Local Anesthesia".

Hypercoagulability

It includes:

Venous hypercoagulability (Venous Thrombo-embolism):

a- Hereditary (heritable) causes (thrombophilia):

- Decreased anti-thrombotic proteins:
  - Antithrombin deficiency.
  - Protein C and protein S deficiency.
- Increased prothrombotic proteins:
  - Factor V_{Leiden}
- Other causes.

b- Acquired causes: Virchow's triad

Arterial hypercoagulability:

a- Hereditary (heritable) causes.

b- Acquired causes.

Venous Hypercoagulability (Venous Thrombo-embolism)

Virchow's Triad

Virchow's triad simplifies the risk factors and causes of thromboembolism as follows:

- Hypercoagulable states: hereditary causes, and acquired causes.
- Venous stasis: acquired causes
- Vessel wall abnormalities (damage): acquired causes.

a- Hereditary (Heritable) Causes (Thrombophilia):

1- Decreased Anti-thrombotic Proteins:

	Protein C (and S) Deficiency	Anti-thrombin Deficiency
Causes	Protein C is a vitamin K dependant anticoagulant synthesized in the liver causing: • Inhibition of activated factors V and VIII. • Stimulation of fibrinolysis. So, inherited protein C (and S) deficiency causes hypercoagulation. N.B.: Acquired Protein C deficiency is due to: liver diseases, nephrotic syndrome, DIC, adult respiratory distress syndrome, postoperative period, postpartum, and hemodialysis. During the first days of warfarin treatment, before inhibition of vitamin K has decreased factors VII, IX, and XI sufficiently to provide the intended anticoagulation, modest suppression of protein C synthesis may compound the already subnormal protein C levels, resulting in paradoxical hypercoagulability.	Anti-thrombin causes: • Inhibition of activated factors II and V. So, inherited antithrombin deficiency (autosomal dominant) causes hypercoagulation. N.B.: Acquired antithrombin deficiency is due to: liver diseases, nephrotic syndrome, DIC, drugs as heparin, oral contraceptive pills (estrogen type).
Clinical Picture	• Recurrent thrombo-embolic diseases as myocardial or cerebral infarctions and pulmonary embolism. • Resistance to the anticoagulation effect of heparin.	
Investigations	• Routine coagulation tests (PT, PTT, and BT) are **normal.**	• **Decreased antithrombin** concentration in the plasma.
Treatment	• **Oral anticoagulants** to prevent thrombosis. • **Regional anesthesia** is preferred because general anesthesia increases coagulation • **FFP**.	• **Oral anticoagulants.** • **Anti-thrombin administration** as antithrombin concentrates, or FFP for acute management.

2- Increased Prothrombotic Proteins:

- **Factor V_{Leiden}:**

It is a hereditary disease producing abnormal factor V called factor V_{Leiden}, which differs from factor V in a single amino acid substitution rendering it refractory to inactivation by the activated protein C. The latter produces anticoagulation effect. Therefore, V_{Leiden} stays active in the circulation for a longer time with increased thrombin generation. This increases the risk of venous thromboembolism 5-7-fold in heterozygous up to 80-fold in homozygous trait.

- **Prothrombin Gene Mutation (G20210A).**

3- Other Hereditary Causes:

- Dysfibrinogenemia.
- Hyper-homocysteinemia.
- Methylene-tetra-hydro-folate reductase (MTHFR) gene mutation (C677T).

b- Acquired Causes:

1- Venous Stasis: such as

- Immobilization.
- Advanced age.
- Congestive heart failure.
- Obesity.
- Surgery.
- Atrial fibrillation.

2- Vessel Wall Abnormalities:

- Trauma.
- Peripheral vascular disease.
- Artificial surfaces as vascular grafts, heart valves, indwelling catheters.
- Coronary artery disease.
- Vasculitis.
- Varicosities.
- Diabetes mellitus.
- Previous thrombosis.

3- Hypercoagulable States:

a- Abnormalities of physiologic anti-thrombotic mechanisms:

- Acquired protein C and S deficiency.
- Plasminogen activator deficiency.
- Acquired antithrombin deficiency.
- Defective or deficient plasminogen.

b- Abnormalities of coagulation and fibrinolysis:

- Malignancy (due to release of procoagulant factor (s) by the tumor, endothelial damage by the tumor invasion, and blood stasis) e.g., adenocarcinoma of pancreas, colon, stomach and ovaries are the leading tumors associated with thromboembolic events.
- Oral contraceptives (estrogen type).
- Pregnancy.
- Tamoxifen.
- Lupus anticoagulant/anti-phospholipid antibody syndrome.
- Hormone replacement therapy.
- Prothrombin complex concentrate solution.
- Nephrotic syndrome due to renal loss of antithrombin or protein C and factor XII deficiency.

c- Abnormalities of platelets:

- Myelo-proliferative disorders.
- Hyperlipidemia.
- Heparin associated thrombocytopenia.
- Paroxysmal nocturnal hemoglobinuria.
- Diabetes mellitus.
- Thrombotic thrombocytopenic purpura.

d- Hyperviscosity:

- Polycythemia.
- Leukemia.
- Sickle cell anemia.
- Leuko-agglutinin
- Hyper-gamma-globulinemia.

Risk factor stratification of deep venous thrombosis is discussed in chapter "Respiratory Diseases".

Arterial Hypercoagulability

Risk factors of arterial thrombosis are different from that of venous thrombosis. They include:

- Hereditary factors.
- Hypercoagulable states.
- Vessel wall injury.

N.B.: Other components of Virchow's triad as stasis and most of hypercoagulable states are not risk factors for arterial hypercoagulability.

a- Hereditary (Heritable) Causes:

- Enhancement of the function of platelet glycoprotein Ib, which mediates platelet adhesion to the vWF under high shear causing more thrombosis.
- Mutation in platelet glycoprotein IIIa (known as $P1^{A2}$ polymorphism) (part of the glycoprotein IIb/IIIa complex critical in platelet-platelet binding), causing more thrombosis.

b- Acquired Causes:

1- Vessel wall abnormalities (endothelial damage):

- Anterior wall infarction.
- Critical atherosclerotic lesions: They produce a high shear flow and activate platelets.

2- Hypercoagulable states:

- Myelo-proliferative disorders as polycythemia vera.
- Paroxysmal nocturnal hemoglobinuria
- Anti-phospholipid antibodies.

Arterial thrombosis causes:
- Cerebral thrombosis resulting in cerebral stroke and/or
- Coronary thrombosis resulting in myocardial infarction.

They are discussed in their corresponding chapters.

Disorders of Platelets

Physiological Considerations

• Platelets are derived from megakaryocytes, which fragment, releasing up to 4000 platelets. Immature platelets spend 24 hours in the spleen before finally entering the circulation, where they have a lifespan or 2 weeks.

• Platelets have many functions; adhesion reaction, release (degranulation) reaction, aggregation (fusion) reaction, and platelet procoagulant activity (see above).

• Since a platelet has a life span of approximately 9-10 days, about 15 000 -45 000 platelets/μL must be produced each day to maintain steady state.

Disorders of Decreased Platelet Count or Function

They include • Thrombocytopenia.
• Thrombasthenia.

Thrombocytopenia

Thrombocytopenia is decreased platelet count < 100-150 × 10^9/Liter.

Causes:

a- Inherited (Congenital):

• May-Hegglin anomaly: It is autosomal dominant with giant platelets.
• Congenital hypoplastic thrombocytopenia with absent radii (TAR syndrome): It is autosomal recessive.
• Fanconi syndrome (see before).
• Wiskott-Aldrich syndrome: It is x-linked, and consists of eczema, immunodeficiency, and thrombocytopenia.
• Alport's syndrome: It is autosomal dominant, associated with deafness and nephritis.
• Bernard-Soulier syndrome.

b- Acquired:

Decreased Production:

1- Bone Marrow Infiltration or Replacement:

• Leukemia and lymphoma.
• Metastatic carcinoma.
• Aplastic anemia.

2- Toxic or Environmental Exposures:

• Alcohol.
• Radiation.
• Chemotherapy.
• Chemicals.
• Thiazide diuretics.

3- Ineffective Hematopoiesis:

• Vitamin B_{12} or folate deficiency.
• Myelo-dysplastic syndrome.
• Paroxysmal nocturnal hemoglobinuria

4- Infections:

• Viral: human immunodeficiency virus, hepatitis, cytomegalovirus.
• Fungal: histoplasmosis.
• Acid fast organisms: tuberculosis.
• Bacterial sepsis.

5- Acquired Amegakaryocytic Thrombocytopenia.

Increased Destruction or Utilization:

1- Mechanical:

• Abnormal heart valves.
• Snake bite.
• Cardiopulmonary bypass.
• Fat embolism.
• Vascular devices.
• Vasculitis.
• Renal transplant rejection.
• Burns (> 10% body surface area).
• Giant cavernous hemangiomas (Kasabach-Merritt syndrome).

• Hemolytic uremic syndrome: It is often seen in children who present with bloody diarrhea secondary to Escherichia coli. It is presented with acute renal failure, anemia, and thrombocytopenia.
• **DIC:** Thrombocytopenia can occur as a part of DIC with deficiency of other clotting factors, but it can occur alone and so called, **platelet DIC** i.e., there is activation of platelets without activation of the coagulation system.
• Catheter-induced thrombocytopenia: It occurs especially with a pulmonary artery catheter of poly-vinyl chloride material, which is thrombogenic, causing thrombus formation. It produces platelet consumption in spite of the heparin saline used. A heparin bonded pulmonary artery catheter is now available.
• **Thrombotic thrombocytopenic purpura (TTP):** It is accompanied with disseminated intravascular aggregation of platelets causing thrombocytopenia.
Causes: familial, idiopathic, complication of bone marrow transplantation, or drugs as interferon-α, cyclosporin, or ticlopidine.
Clinical picture: severe microangiopathic hemolytic anemia (resulting in fever and jaundice), multiple small vessel occlusions (platelet thrombi) involving the kidney (resulting in renal impairment), brain (resulting in focal cerebral lesions up to coma and fits), skin, and distal extremities. Mortality is 60-80% in the 1st 10 days of the disease. It is treated by anti-platelets and exchange plasmapheresis.

2- Sequestration (hypersplenism or hypothermia).

3- Massive blood transfusion: which causes dilutional thrombocytopenia as stored blood contains only 20% of alive-platelets after 3 days of storage.

4- Immunological:

• **Idiopathic (Autoimmune) Thrombocytopenic Purpura (ITP)** due to anti-platelet immunoglobulins that bind to the platelet membrane causing premature destruction.
Treatment:
  ▫ Corticosteroids: high-dose in the first 3 days to prevent change to chronic state.
  ▫ Immuno-suppressive agents e.g., vincristin.
  ▫ I.v. immunoglobulins can be used before surgery.
  ▫ Platelet transfusion/8-12 hours regardless of the effect on the platelet count. Even when there are no post-transfusion increments, sufficient numbers of the transfused platelets may survive to improve hemostasis.
  ▫ Splenectomy in chronic cases which do not respond to corticosteroids.
• Drug-induced antibodies such as quinidine, quinine, abciximab, α-methyldopa, sulfonamides, gold salts, and heparin. These drugs act as haptens to trigger antibody formation, which bind to the platelet surface.
• Immune complexes.
• Systemic lupus erythematosus and anti-phospholipid antibody syndrome.
• Neoplastic diseases as chronic lymphatic leukemia or Hodgkin's disease.
• Post-transfusion purpura, which occurs 2-10 days after whole blood transfusion.
• Neonatal allo-immune thrombocytopenia.
• Viral-associated (human immunodeficiency virus, infectious mononucleosis, cytomegalovirus).
• Pregnancy (gestational thrombocytopenia).
• HELLP syndrome in severe preeclampsia. It is discussed in the chapter of "Obstetrics".
• Autoimmune thrombocytopenia.
• Malaria (probably immune).
• Bacterial sepsis (probably immune).

N.B.: **Artifactual Thrombocytopenia:** It occurs due to:
  • Pseudo-thrombocytopenia (due to in vitro platelet clumping in the presence of EDTA anti-coagulant).
  • Platelet satellitism around neutrophils.
  • Presence of giant platelets that may not be counted as platelets by automated cell counters. This is detected by blood film examinations.

Thrombasthenia

Thrombasthenia is platelet dysfunction.

a- Inherited (Congenital):

Function	Disorder
Adhesion	• Von Willebrand's disease (the most important). • Bernard-Soulier syndrome (GPIb deficiency)
Release	• Grey platelet syndrome • Storage pool syndrome • Arachidonic acid pathway abnormalities • Defective Ca^{++} mobilization • Wiskott-Aldrich syndrome (defective cytoskeletal regulation)
Aggregation	• Glanzmann's thrombasthenia (GPIIb/IIIa deficiency) • Afibrinogenemia (although the defect is extrinsic to platelet, it affects platelet function).
Procoagulant activity	• Decreased platelet factor III activity. • Scott syndrome (asymmetry of platelet phospholipids).

b- Acquired:

- **Uremia.**
- **Liver failure.**
- **Cardiopulmonary bypass:** as there is a change in the media in which platelets circulate.
- **DIC:** as there is consumption of platelets (thrombocytopenia) and accumulation of fibrinogen degradation products, which interfere with platelet function (thrombasthenia).
- **Myelo-proliferative** or myelo-dysplastic syndromes as polycythemia vera, myeloid metaplasia, idiopathic myelo-fibrosis, essential thrombocythemia, and chronic myelogenous leukemia. Some of these patients even have very high platelet counts, but demonstrate abnormal bleeding or tendency to arterial or venous thrombosis or even both due to abnormal platelet functions.
- **Massive transfusion of stored blood:** as there is platelet dysfunction due to depletion of energy stores especially ATP, which return to normal function after 8-20 hours.
- **Drug induced:**
  - **Aspirins and non-steroidal anti-inflammatory drugs (NSAIDs)** e.g., naproxen, ibuprofen, indomethacin, piroxicam, ketorolac, or phenylbutazone, which decrease prostaglandin synthesis by irreversible inhibition of cyclo-oxygenase enzyme (important for platelet release of ADP). The effect occurs 3 hours after one tab of 300 mg aspirin and lasts 2 weeks. Therefore, **stop aspirin and NSAIDs 2 weeks before surgery.**
  - **Dipyridamole.**
  - **Heparin.**
  - **Alcohol.**
  - **Antiplatelet drugs as clopidogrel, ticlopidine, abciximab.**
  - **Fibrinolytic agents** as epsilon amino-caproic acid.
  - **Colloids** as dextran and hydroxyethyl starch. The latter is less likely to produce thrombasthenia which may occur if the dose exceeds 2 liters of the 6% solution.
  - **Antibiotics** as high dose penicillin, β-lactam antibiotics, or some cephalosporins.
  - **Oncologic drugs** as daunorubicin and mithramycin.
  - **Cardiovascular drugs** as β- blockers, Ca^{++} channel blockers, nitroglycerin, nitroprusside, or quinidine.
- **Certain foods and food additives** (vitamin C, E, omega-3 fatty acids, Chinese black tree fungus) also inhibit cyclo-oxygenase enzyme.
- **Hypothermia < 35°C.**
- **Acidosis pH < 7.3.**

Clinical Picture of Thrombocytopenia and Thrombasthenia:

1- Bleeding manifestations: They depend on the level of platelet count.

Platelet Count (/μL)	Clinical Picture
> 100 000	No increase in bleeding
50 000-100 000	Minimal bleeding even with surgery unless platelet dysfunction is present.
30 000- 50 000	Increased bleeding with surgery or trauma.
20 000- 30 000	Occasionally associated with easy bruising and ecchymosis or other **minor spontaneous** bleeding. Sometimes, petechial purpura at the site of the usual trauma as below the knees, oral mucosa (with blood-filled blisters), constricting clothing sites...etc. Oozing at the operation and venipuncture site.
10 000- 20 000	**Spontaneous** epistaxis, petechiae (pin-point hemorrhage) (figure 30-9), menorrhagia, gum bleeding.
< 10 000	Increased gastrointestinal blood loss, spontaneous life threatening bleeding (e.g., intracranial hemorrhage, hematuria, melena, eye fundal hemorrhage, or hematemesis) especially if it is associated with an underlying vascular defect or a second hemostatic defect (including aspirin ingestion).

2- Manifestations of the cause:

- ITP: Trans-placental passage of antibiotics occurs, causing **neonatal hemorrhage**.
- TTP: Thrombus formation and hemolytic anemia occur (see above).



Figure 30-9: Petechiae

Investigation:

1- There is **prolonged bleeding time.**

2- Platelet count: • If there is a **decreased platelet count**, it is **thrombocytopenia**.
• If there is a **normal platelet count**, it is **thrombasthenia**.

3- Thromboelastography.

4- A peripheral smear made from fresh non-anticoagulated blood may detect morphologic platelet abnormalities or absence of platelet aggregation.

Treatment:

1- Treatment of the cause e.g., stoppage of the causative drug.

2- Platelet transfusion: 1 unit for each 10 kg body weight. It is indicated when platelet count is < 50 000 /μL.

- For minor procedures such as central catheter insertions or biopsies, the platelet count should be raised to at least 50 000/μL.
- For major procedures as those in critical sites as brain or eyes, lumbar puncture, or epidural anesthesia, the platelet count should be raised to at least 100 000/μL.

3- Desmopressin for platelet dysfunction.

Disorders of Increased Platelet Count or Function (Thrombocythemia)

Definition: Platelet counts often exceed 800 000/μL.

Causes:

a- Reactive:

- Hemorrhage especially prolonged low level bleeding
- Trauma or postoperative period.
- Chronic infection.
- Malignancy.
- Chronic iron deficiency.
- Connective tissue diseases e.g., rheumatoid arthritis.
- Post-splenectomy with continuing hemolytic anemia.

b- Endogenous:

- Essential Thrombocythemia (idiopathic).
- Myelo-proliferative disorders such as polycythemia vera, myelo-sclerosis or myelo-fibrosis, chronic granulocytic leukemia.

Clinical Picture:

The major risk is thrombosis.

Investigations:

1- Increased platelet count.
2- Blood film shows abnormal large platelet or megakaryocytic fragments.
3- Abnormal platelet function tests (see later).

Treatment:

1- Mobilization of the patient.
2- Prophylactic aspirin 150 mg oral/12 hours or low molecular weight heparin 5000 IU subcutaneous once.
3- Dipyridamole 300-600 mg/8 h orally.
4- Radioactive phosphate or alkylating agents are used to keep platelet counts low.

Disorders of White Blood Cells (WBCs)

Physiological Considerations

WBCs are divided into two broad categories:

a- Phagocytes: include neutrophils, polymorphs, eosinophils, basophils, and monocytes.

Neutrophils are slightly larger than RBCs, having a diameter of 12-15 μm. They have a characteristic multi-lobular nucleus and a cytoplasm filled with fine granules (enzymes and lysosomes). In time of sepsis and stress, there is an increase in the number of immature neutrophils in the circulation, known as "band" or "juvenile" forms.

b- Lymphocytes: are small cells (7-15 μm in diameter). These subdivide into T and B lymphocytes. The lymphocyte population increases following antigenic stimulation.

Disorders of Decreased White Blood Cell Count

1- Neutropenia (Granulocytopenia)

2- Abnormalities of Phagocytosis

They are discussed in the chapter of "Immune System Diseases".

Disorders of Increased White Blood Cell Count

1- Neutrophilia

It is discussed in the chapter of "Immune System Diseases".

2-Leukemia

It is the uncontrolled production of leukocytes owing to cancerous mutation of lymphogenous cells in lymph nodes (lymphocytic leukemia) or myelogenous cells in bone marrow (myeloid leukemia).

It leads to expanding mass of cells that infiltrate the bone marrow, rendering patients functionally aplastic. Anemia may be profound. Eventually, bone marrow failure is the cause of fetal infections or hemorrhage due to thrombocytopenia. Leukemia cells may also infiltrate the liver, spleen, lymph nodes, and meninges, producing signs of dysfunction at these sites. Extensive use of nutrients by rapidly proliferating cancerous cells depletes amino acids, leading to patients fatigue and metabolic starvation of normal tissues.

Acute Lymphoblastic Leukemia:

- It accounts for approximately 15% of all leukemia in adults.
- Central nervous system dysfunction is common.
- Life-threatening opportunistic infection including that due to Pneumocystis carinii and cytomegalovirus is common.
- Chemotherapy can cure as many as 70% of children and 25% to 45% of adults.

Chronic Lymphocytic Leukemia:

- It accounts for approximately 25% of all leukemia in adults. It rarely occurs in children.
- Bone marrow is infiltrated by lymphocytic infiltrates.
- Clinical picture includes autoimmune hemolytic anemia, hypersplenism, pancytopenia, thrombocytopenia, and lymph node enlargement.
- Chemotherapy, corticosteroids, and radiotherapy are used in treatment.

Acute Myeloid Leukemia:

- It is characterized by an increase in the number of myeloid cells in bone marrow and arrest their maturation, frequently resulting in hematopoietic insufficiency (granulocytopenia, thrombocytopenia, and anemia).
- Clinical picture depends on the organs affected. It includes significant or life-threatening infection, fatigue, bleeding gums or nose, pallor, headache, dyspnea on exertion, hepatomegaly, splenomegaly, lymphadenopathy, and infiltration of eyes, bones, and central nervous system.
- Hyper-leukocytosis (more than 100,000 cells/mm^3). Hyperuricemia and hypocalcemia are common.
- Chemotherapy is used in treatment. Bone marrow transplantation is indicated in patients not responding to chemotherapy.

Chronic Myeloid Leukemia:

- It is similar to acute myeloid leukemia with splenomegaly. High leukocytic counts may predispose to vascular occlusion.
- Chemotherapy leukopheresis, splenectomy, and allogenic stem cell transplantation are used for treatment.

Bone Marrow Transplantation (Hematopoietic Stem Cell Transplantation):

Types:

- **Autologous bon marrow transplantation:** It entails collection of the patient's own bone marrow for subsequent reinfusion.
- **Allogenic bone marrow transplantation:** It uses bone marrow or peripheral blood elements from an immuno-compatible donor.

Technique:

- Regardless of the type of bone marrow transplantation, recipients must undergo a preoperative regimen designed to achieve functional bone marrow ablation by a combination of total body radiation and chemotherapy.
- Bone marrow is usually harvested by repeated aspirations from the posterior iliac crest.
- For allogenic bone marrow transplantation with major AB incompatibility between donor and recipient, it is necessary to remove mature erythrocytes from the graft to avoid a hemolytic transfusion reaction. Removal of T cells from the allograft can decrease the risk of graft-versus-host disease.
- Processing of the harvested bone marrow (eradicating malignant cells, removing incompatible erythrocytes) may take 2-12 hours.
- The condensed bone marrow volume (approximately 200 mL) is then infused into the recipient through a central venous catheter. From the systemic circulation, the bone marrow cells pass into the recipient's bone marrow, which provides the micro-environment necessary for maturation and differentiation of the cells.
- The time necessary for bone marrow engraftment is usually 10 to 28 days, during which time protective isolation of the patient may be required. While awaiting engraftment, it may be necessary to administer

platelets to maintain the count above 20,000 cells/mm^3 and erythrocytes to maintain the hematocrit above 25%.

Choice of Anesthesia during Bone Marrow Transplantation:

- Either general or regional anesthesia can be used during aspiration of bone marrow from iliac crests.
- Nitrous oxide is usually avoided due to the possibility of bone marrow depression associated with this drug.
- Blood replacement may be necessary, either with autologous blood transfusion or by reinfusion of separated erythrocytes obtained during the harvest.

Complication of Bone Marrow Transplantation:

1- Graft-Versus-Host Disease:

It occurs when immunologically competent cells in the graft target antigens on the recipient's cells.

Clinical Picture:

It is presented in 2 clinical entities:

a- Acute disease that occurs during the first 30-60 days after bone marrow transplantation.

b- Chronic disease that occurs at least 100 days after bone marrow transplantation.

Manifestations include:

- Pancytopenia and immunodeficiency.
- Maculopapular rash, erythroderma, and desquamation.
- Oral ulceration and mucositis.
- Esophageal ulceration.
- Diarrhea.
- Hepatitis with coagulopathy.
- Bronchitis obliterans.
- Interstitial pneumonitis.
- Pulmonary fibrosis.
- Renal failure.

2- Graft Rejection:

It occurs when immunologically competent cells of host origin destroy the cells of donor origin.

3- Pulmonary Complications:

They include infection, adult respiratory distress syndrome, chemotherapy-induced lung damage and interstitial pneumonitis. It occurs after allogenic bone marrow transfusion.

4- Veno-occlusive Disease of the liver:

It occurs after allogenic and autologous bone marrow transplantation. It is associated with jaundice, tender hepatomegaly, ascites, and weight gain. Finally progressive hepatic failure occurs.

N.B.: Hodgkin's Lymphoma:

Causes and Risk factors:

- Epstein-Barr virus infection.
- Genetic factors.
- Environmental factors.

e

- Impaired immunity e.g., patients after organ transplantation or patients who are human immunodeficiency virus positive.

Clinical Picture:

- Lymph adenopathy in predictable areas such as cervical and anterior mediastinal adenopathy
- Generalized and severe pruritis.
- Night sweats and unexplained weight loss.
- Peripheral neuropathy and spinal compression due to tumor growth.

Investigations:

- Lymph node biopsy is diagnostic.
- Computed tomography and positron emission tomography scanning of the chest, abdomen, and pelvis for tumor staging.
- Bone marrow biopsy.

Treatment:

- Radiation therapy.
- Chemotherapy.

Hematological Laboratory Tests

They include coagulation screen tests and more sophisticated tests, which are used to confirm the diagnosis.

Indications of Coagulation Screen Tests:

a- Elective:

1- A **suspicious history** (bleeding after a wound, previous surgery or easy bruising, suspected DIC).
2- **Massive blood transfusion**.
3- A **family history** due to inherited disorders.
4- **Patient receiving anticoagulants** as warfarin, heparin, aspirin… etc.
5- Inter-current illness as obstructive jaundice, liver disease, uremia...etc.

b- Emergency or Intraoperative:

- **Excessive bleeding** despite apparent vascular integrity.

Blood Samples

Measurement of coagulation tests e.g., PT and aPTT, involves decalcified plasma (collected in citrate) i.e., removal of calcium from the plasma by the effect of citrate.
For PT and aPTT, a phospholipid substitute as thromboplastin (acts as an activating agent) and calcium are added.
For TT, excess thrombin is added to the decalcified plasma (a phospholipid is not required).
After that, the time for visible clot formation is determined using an automated system.

A) Tests of Coagulation:

Test	Normal Value	Significance
a) Screening Tests: 1- Prothrombin Time (PT)	12-14 sec	It tests the extrinsic (III and VII) and common pathways (I, II, V, and X).
2- Activated Partial thromboplastin Time (aPTT)	35-45 sec	It tests the intrinsic (VIII, IX, XI , and XII) and common pathways (I, II, V, and X).
3- Thrombin time (TT)	12-20 sec	It tests the common pathway (I, and II). It is affected by heparin.
4- International Normalized Ratio (INR)	1-1.2	It assesses warfarin therapy • Therapeutic range for atrial fibrillation, DVT, pulmonary embolism, and tissue heart valves is = 2-3. • Therapeutic range for mechanical heart valves is = 3-4.5. It assesses factor VII activity (it has a short $t_{1/2}$); so, other factors may be low as II, IX, and X while INR is slightly prolonged (i.e., it represents normalization of factor VII). It expresses the PT as it compares observed results against a reference thromboplastin to minimize inter-laboratory variability owing to different sensitivities of thromboplastin reagents.
b) More Sophisticated Tests: 1- Activated Clotting Time (ACT)	70-180 sec	It is used intraoperatively in cardiac surgery. It is discussed in more details in chapter "Cardiac Surgery".
2- Thromboelastography		It is discussed later.
3- Reptilase Time		It detects deficiency or defects of fibrinogen. It is similar to TT, but is unaffected by heparin.
4- Stypven Time (Russell Viper Venom Time)		It differentiates factor VII from factor X deficiency (it is abnormal in factor X deficiency).
5- Dilute Russell Viper Venom Time		It detects lupus anticoagulants. It is affected by heparin.
6- Dilution test (1:1)		A mixture of patient plasma with normal plasma in equal quantities (1:1 dilution) is performed. There should be normalization of prolonged coagulation time if the cause is deficiency of one or more of the coagulation factors. Failure of a prolonged coagulation time to correct after mixture implies the presence of a circulating inhibitor of coagulation to specific factors such as heparin or to phospholipids.
7- Factor Assays (60-100%)		It detects deficiency of one or more of the coagulation factors.

N.B.: Coagulation times shorter than normal occur frequently, particularly if there are higher than normal levels of any of the factors measured by the test (especially factor VIII), which may mask deficiencies of other factors.

B) Tests of Platelets:

Test	Normal Value	Significance
I) Screening Tests:		
1- Platelet Count	150 000-450000/μL	It detects quantitative abnormalities of platelets (see below). Even minimal platelet activation, as with a difficult blood draw, can cause platelet clumping and result in artifactually decreased counts on automated analyzers. Most clinical laboratories examine stained blood films for clumping if the platelet count is < 100 000/μL.
2- Bleeding Time (BT)	3-10 min	It is prolonged in thrombocytopenia, thrombasthenia, severe anemia, abnormal vascular integrity, and improper techniques. Method: A standardized incision 9 mm long and 1 mm deep is made on the volar surface of the forearm, with back-pressure maintained by inflating a blood pressure cuff on the upper part of the arm to 40 mm Hg of pressure. Excess blood is blotted away every 30 seconds with filter paper without disturbing the wound edge. Validity: Although this test is the single best predictor of functional platelet disorders, the test must be performed in a standardized controlled setting, is difficult to control, and is often not readily available.
II) More Sophisticated Tests:		
1- Aggregation Test		It detects impaired platelet aggregation in response to platelet agonists e.g., thrombin, epinephrine, adenosine di-phosphate (ADP) and ristocetin. It can localize the defect based on the pattern of abnormal aggregation.
2- Ristocetin Cofactor Assay		It detects decreased quantity or function of vWF in patient's plasma.
3- Platelet function Analysis (Assay)		Anticoagulated whole blood is exposed to high-shear flow conditions, and membrane-bound collagen coated with either adenosine di-phosphate (ADP) or epinephrine initiates the release of platelet granules and membrane adhesion. The time to instrument aperture occlusion as a result of platelet thrombus formation is measured.

NB.: Normal platelet count can be expressed as:

150-450 X 10^9/L,
150-450 X 10^6/mL (or cc), or
150-450 X 10^3/μL (or mm^3).

C) Tests of Fibrinolysis:

Test	Normal Value	Significance
I) Screen Tests:		
1- Fibrin (and Fibrinogen) Degradation Products (FDPs)	< 10 μg/mL	It indicates accelerated intravascular fibrinolysis. It is a nonspecific test. Results > 40 μg/mL indicate DIC.
2- Fibrinogen Level	150-400 mg/dL	It indicates accelerated intravascular fibrinolysis or deficiency of fibrinogen. It is a nonspecific test.
3- D-dimer test		It measures blood levels of D-dimers fragments that are released when plasmin cleaves cross-linked fibrin formed only if activation of factor XIII has resulted in cross-linkage of fibrin polymers. It is elevated in DIC, fibrinolysis, deep venous thrombosis, and pulmonary embolism. It is not elevated in primary fibrinolysis because the fibrin is not cross-linked.
II) More Sophisticated Tests:		
1- Euglobulin lysis time		It measures the action of plasminogen activators and plasmin in blood. It indicates accelerated fibrinolysis.
2- Protamine Sulfate Test		It indicates presence of circulating fibrin monomers.

Thromboelastography (TEG)

It was first developed by Hartert in 1948.

Idea:

TEG provides a method for **evaluation of the whole coagulation** system **from the initial clot formation to clot retraction or dissolution.** It measures the **thrombo-dynamic (visco-elastic) properties** of the whole coagulation process over time. The blood is induced to clot under a low shear environment resembling sluggish venous flow.

Indications:

1- It **quantitavely and qualitatively assesses the overall coagulation profile** of a blood sample (interpreted in terms of a normal, hypo- or hyper-coagulable state) and the degree of lysis. The etiology of a coagulopathy may be obtained by analyzing the curves of the TEG.

2- It **guides therapy** in the form of fresh frozen plasma (FFP), cryoprecipitate, platelets, or antifibrinolytics. In addition, these therapies can first be applied in vitro to confirm their effects on the patient's blood sample before administration of treatment.

In addition, to the inactivated TEG, activation reagents shorten the result time and improve precision, and can allow differential diagnosis.

The Thromboelastogram:

It is the instrument of the TEG.

Components:

- A rotating piston (pin) is suspended in a cylindrical cup (cuvette) filled with heated blood at 37 °C. The piston is attached to a calibrated torsion wire.
- As clot formation proceeds, the rotation of the piston is affected and characteristic curves are generated (figure 30-10).

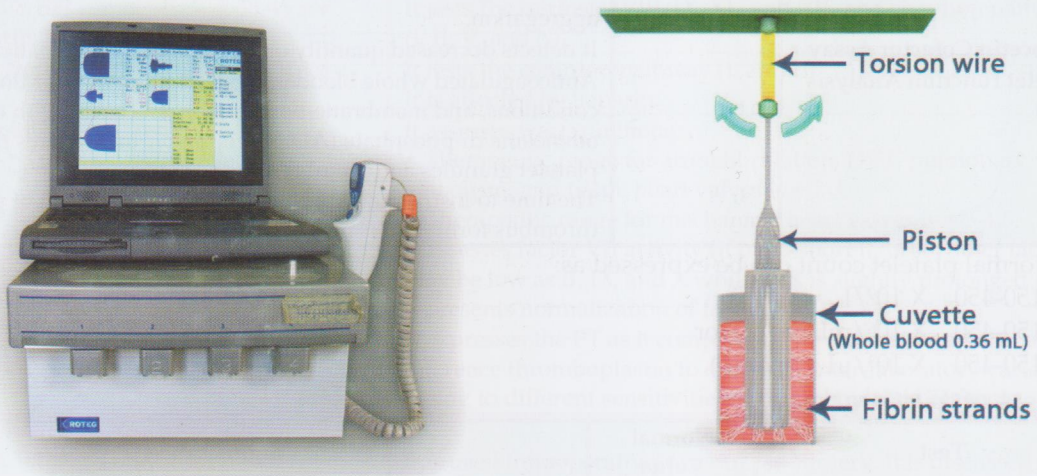


Figure 30-10: TEG

Technique:

- A small sample of blood (0.36 mL) is placed in the cup and allowed to clot as the cup oscillates through an angle of 45°. Each rotation cycle lasts 10 seconds.
- The elastic shear properties of the sample are measured as fibers composed of fibrin and platelets are formed, and attach the cup to the pin, which becomes monitored for motion.
- The strength and rate of these fibrin-platelet bonds affect the magnitude of the pin motion such that strong clots move the pin directly in phase with the cup motion. Thus, the magnitude of the output is directly related to the strength of the formed clot.
- As the clot retracts or lyses, these bonds are broken and the transfer of cup motion is diminished.
- The rotation movement of the pin is converted to a mechanical signal that can be monitored by a computer. The resulting hemostatic profile (curve) is a measure of the time taken for the first fibrin strand to be formed, and the kinetics of clot formation, its strength, and dissolution.

Analysis of Thromboelastograph's Curves:

Normal Measured Parameters: (figure 30-11)

Parameter	Definition	Normal Value	Significance
Reaction time (R)	• It is the reaction time, which represents the period from placing the blood sample in the cup until the initial fibrin formation. It represents the clotting time. • It may be accelerated by adding celite to the TEG sample in the cuvette.	7-14 min	• It is prolonged by a deficiency of one or more plasma coagulation factors, anticoagulation (heparin or severe hypofibrinogenemia). • It is shortened in hypercoagulability.
K value	• It is the coagulation time, which measures the speed required to clot from R time to reach 20 millimeters of blood clot strength.	3-7 min	• K value is prolonged and α angle is decreased by any factor slowing clot generation such as coagulation factor deficiencies or heparin anticoagulation.
Clot Formation Rate (α angle)	• It measures the rapidity of fibrin build up and cross-linking i.e., solid clot formation. It is the angle formed by the slope of the TEG tracing from the R to the K value.	40-60°	
Maximum Amplitude (MA)	• It represents the maximum clot strength and is a direct function of the maximum dynamic properties of fibrin and platelet bonding. • It is a direct function of fibrinogen concentration, platelet count and quality, and the interaction of fibrin and the platelet plug.	40-60 mm	• It is decreased by either qualitative or quantitative platelet dysfunction or decreased fibrinogen concentration.
Whole Blood Clot Lysis Index (Fibrinolytic Index)	a- For Non-computerized TEG: It is the amplitude of the tracing 60 min after the MA. It is expressed as a percentage of MA and it represents the amount of clot retraction or lysis (LY 60%). b- For Computerized TEG: It reports LY 30 and LY 60%. These measure the reduction in the area under the TEG tracing from the time of the MA until 30 (LY 30, normal < 7.5%) or 60 (LY 60, normal < 15%) minutes after the MA.	> 0.85 (> 85%)	
Whole Blood Clot Lysis Time (F)	• It is the time of the whole clot lysis	> 300 min	

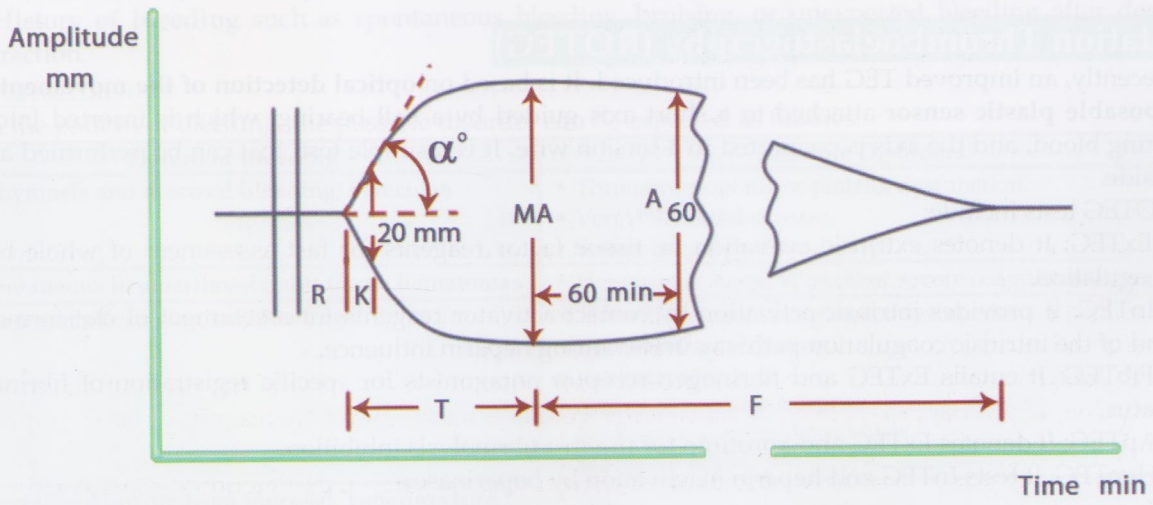
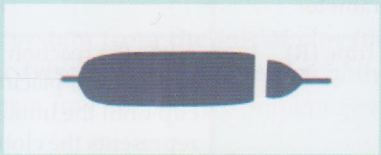
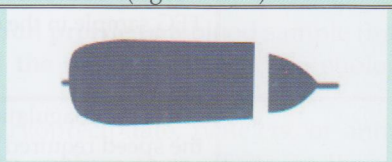
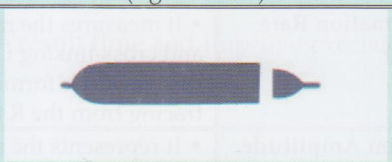
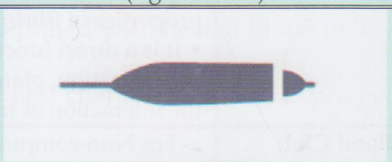
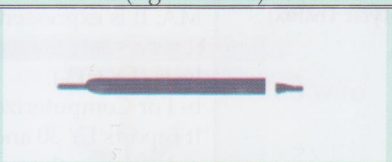
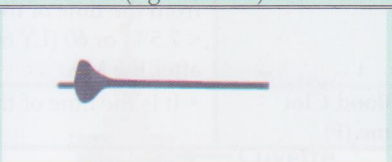


Figure 30-11: TEG curve

Qualitative Analysis of Thromboelastograms:

	Measured parameters	Curve
Normal (figure 30-12)	R, K, MA and Angle = Normal	The onset The end  (figure 30-12)
Hyper-coagulation (figure 30-13)	R/K = Decreased MA and Angle = increased	 (figure 30-13)
Thrombocytopenia (figure 30-14)	R = Normal K = Prolonged MA = Decreased	 (figure 30-14)
Heparin (figure 30-15)	R & K = Prolonged MA and Angle = Decreased	 (figure 30-15)
No platelet function (figure 30-16)	R = Prolonged MA and Angle = Decreased	 (figure 30-16)
Fibrinolysis (figure 30-17)	R = Normal MA = A continuous decrease	 (figure 30-17)

Rotation Thromboelastography (ROTEG)

• Recently, an improved TEG has been introduced. It is based on **optical detection of the movement of a disposable plastic sensor** attached to a short axis guided by a ball bearing, which is inserted into the clotting blood, and the axis is connected to a torsion wire. It is a simple test, that can be performed at the bedside.

• ROTEG tests include:

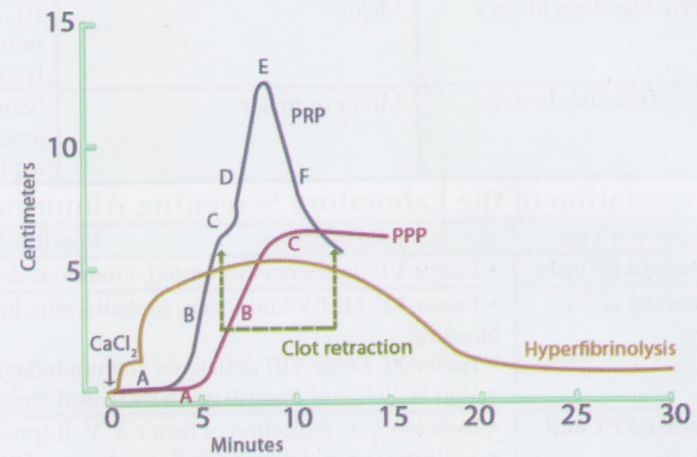
- ExTEG: It denotes extrinsic activation by tissue factor reagents for fast assessment of whole blood coagulation.
- InTEG: It provides intrinsic activation by contact activator reagents for assessment of clot formation and of the intrinsic coagulation pathway under strong heparin influence.
- FibTEG: It entails ExTEG and fibrinogen receptor antagonists for specific registration of fibrinogen status.
- ApTEG: It denotes ExTEG and aprotinin for in-vitro fibrinolysis inhibition.
- HepTEG: It tests InTEG and heparin inactivation by heparinase.

Sonoclot

- It similarly measures the development of the clot's visco-elastic strength.
- It **immerses a rapidly vibrating probe** into a 0.4 mL sample of blood. As clot formation occurs, **impedance to probe movement** and probe vibration through the blood increases, and generates an altered electrical signal and a characteristic clot signature (figure 30-18 and figure 30-19).



Figure 30-18: Sonoclot



PRP = Platelet rich plasma.
PPP = Platelet poor plasma.
(A) Lag period → liquid phase before formation of the clot
(B) Primary wave → clot rate
(C) Shoulder.
(D) Secondary wave → tightening of clot
(E) Peak.
(F) Downward wave.
C + D + E + F → clot retraction

Figure 30-19: The Sonoclot

Clinical Approach of Bleeding Patients

Determination of the bleeding patient can be determined by:

a- History:

- History of **medical illness** such as liver and renal diseases, or myelo-proliferative disorders.
- Presence of **positive family history** to determine the inherited disorders. Sometimes there is negative family history in spite of the presence of an inherited disorder.
- **History of bleeding** such as spontaneous bleeding, bruising, or unexpected bleeding after dental extraction.

b- Examination:

From the pattern of bleeding, the possible disorder can be expected as follows:

Pattern of Bleeding	Possible Disorders
• **Ecchymosis and mucosal bleeding; petechiae**	• Thrombocytopenia or platelet dysfunction. • Von Willebrand disease. • Severe coagulopathies.
• **Spontaneous hemoarthrosis, soft tissue hematomas**	• Hemophilia A and B, or other severe coagulopathies.
• **Post-traumatic or surgical bleeding**	• Thrombocytopenia or platelet dysfunction. • Von Willebrand disease. • Coagulopathies. • Impaired vascular integrity. • Inadequate surgical hemostasis. • Massive injuries.
• **Generalized oozing from mucosal, venepuncture, or surgical sites**	• DIC. • Excessive fibrinolysis. • Severe thrombocytopenia. • Platelet dysfunction.

c- Laboratory Screening Tests:

Recommendation for asking of the laboratory tests depends on the suggested history of the patient and the type of surgery as follows:

Bleeding History	Type of Surgery	Recommended Laboratory Tests
No suggestive history	Minor (dental, skin biopsy)	None
No suggestive history	Major	aPTT, platelet count
Possible bleeding history	Major	PT, aPTT, platelet count, bleeding time, if normal, factor XIII assay and euglobulin clot lysis time are done
Positive bleeding history	Minor or major	Same as above. If negative, thrombin time, factor assays for VIII, IX, XI, α_2-antiplasmin assay, post-aspirin bleeding time.

Interpretation of the Laboratory Screening Abnormalities:

Abnormal Test	Possible Defects
• Increased PT only	• Factor VII deficiency (inherited, vitamin K deficiency, or warfarin effect) or inhibitor.
• Increased aPTT only	• Factor XII, HMW kininogen, prekallikrein, lupus anticoagulant; those do not cause bleeding. • Factor XI, IX, or VIII deficiency (hemophilias); those cause bleeding. • Von Willebrand disease (with increased bleeding time).
• Increased PT and aPTT	• Deficiency or inhibition of factor X, V, II (prothrombin), and fibrinogen. • Multiple factor deficiencies (liver disease, DIC, vitamin K deficiency, high dose warfarin effect, heparin). Warfarin increases PT > aPTT, but heparin increases aPTT > PT.
• Increased bleeding time	• Thrombasthenia. • Thrombocytopenia (with low platelet count). • Improper technique.
• All screening tests normal	• Factor XIII deficiency. • Excessive fibrinolysis • Paraproteinemia. • Vascular defect (including surgical hemostasis). • Supporting tissue abnormalities.

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